COMPARISON OF EFFECTS OF ORAL CLONIDINE AND PREGABALIN FOR HAEMODYNAMIC STABILITY DURING LAPAROSCOPIC SURGERIES- A PROSPECTIVE RANDOMIZED PLACEBO CONTROL STUDY

A STUDY OF 90 CASES

DISSERTATION SUBMITTED

FOR THE DEGREE DOCTOR OF MEDICINE BRANCH – X (ANAESTHESIOLOGY) APRIL **2016**

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI

CERTIFICATE BY THE HEAD OF THE INSTITUTION

This is to certify that the dissertation entitled "**COMPARISON OF EFFECTS OF ORAL CLONIDINE AND PREGABALIN FOR HAEMODYNAMIC STABILITY DURING LAPAROSCOPIC SURGERIES - A PROSPECTIVE RANDOMIZED PLACEBO CONTROL STUDY"** submitted by **Dr.R.BALAKRISHNA** , in partial fulfillment for the award of the degree of Doctor of Medicine in Anaesthesiology by theTamilnadu Dr.M.G.R. Medical University, Chennai , this is a bonafide original research work done by him in the department of Anaesthesiology and Critical Care, Tirunelveli Medical College, under my guidance and supervision during the academic year 2013-2016.

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I, **Dr.R.BALAKRISHNA**, declare that the dissertation has entitled **"COMPARISON OF EFFECTS OF ORAL CLONIDINE AND PREGABALIN FOR HAEMODYNAMIC STABILITY DURING LAPAROSCOPIC SURGERIES - A PROSPECTIVE RANDOMIZED PLACEBO CONTROL STUDY"** has been prepared by me. This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfilment of the requirement for the award of M.D. Degree, Branch X (ANAESTHESIOLOGY) degree examination to be held in April 2016.

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LIST OF ABBREVIATIONS USED

ASA	-	American society of Anesthesiologists
HR	-	Heart rate
SBP	-	Systolic blood pressure
DBP	-	Diastolic blood pressure
MAP	-	Mean arterial pressure
NIBP	-	Non invasive blood pressure
SVR	-	Systemic vascular resistance
ECG	-	Electrocardiogram
CI	-	Cardiac index
IAP	-	Intra abdominal pressure
SPO2	-	Pulse oximeter oxygen saturation
CO2	-	Carbon dioxide
ETCO2	-	End tidal carbon dioxide
MAC	-	Minimum alveolar concentration
COPD	-	chronic obstructive pulmonary disease
IV	-	Intravenous

IM	-	Intramuscular
CNS	-	Central nervous system
GABA	-	Gamma amino butyric acid
GI	-	Gastrointestinal
PONV	-	Post operative nausea vomiting
FDA	-	Food and drug administration
CGRP	-	Calcitonin gene related peptide
VAS	-	Visual analog scale
KG	-	Kilogram
MICS	-	Microgram
PREOP	-	Preoperative
AI	-	After intubation
AP	-	After pneumoperitoneum
PR	-	Pneumoperitoneum release
AE	-	After extubation

CONTENTS

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PROTOCOL TITLE: COMPARISION OF EFFECTS OF ORAL CLONIDINE & PREGABALIN FOR HAEMODYNAMIC STABILITY DURING LAPAROSCOPIC SURGERIES. A PROSPECTIVE RANDAMIZED PLACEBO CONTROL STUDY.

PRINCIPAL INVESTIGATOR: Dr. R. BALAKRISHNA, MBBS.,

DESIGNATION OF PRINCIPAL INVESTIGATOR: POST GRADUATE IN ANAESTHESIOLOGY
DEPARTMENT & INSTITUTION: TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI

Dear ,Dr. R. Balakrishna, MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 10.06.2015.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of the Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
6. At the time of PI's retirement/leaving the institute, the study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
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   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
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   e. Approval for amendment changes must be obtained prior to implementation of changes.
   f. The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g. Any deviation/violation/waiver in the protocol must be informed.

STANDS APPROVED UNDER SEAL

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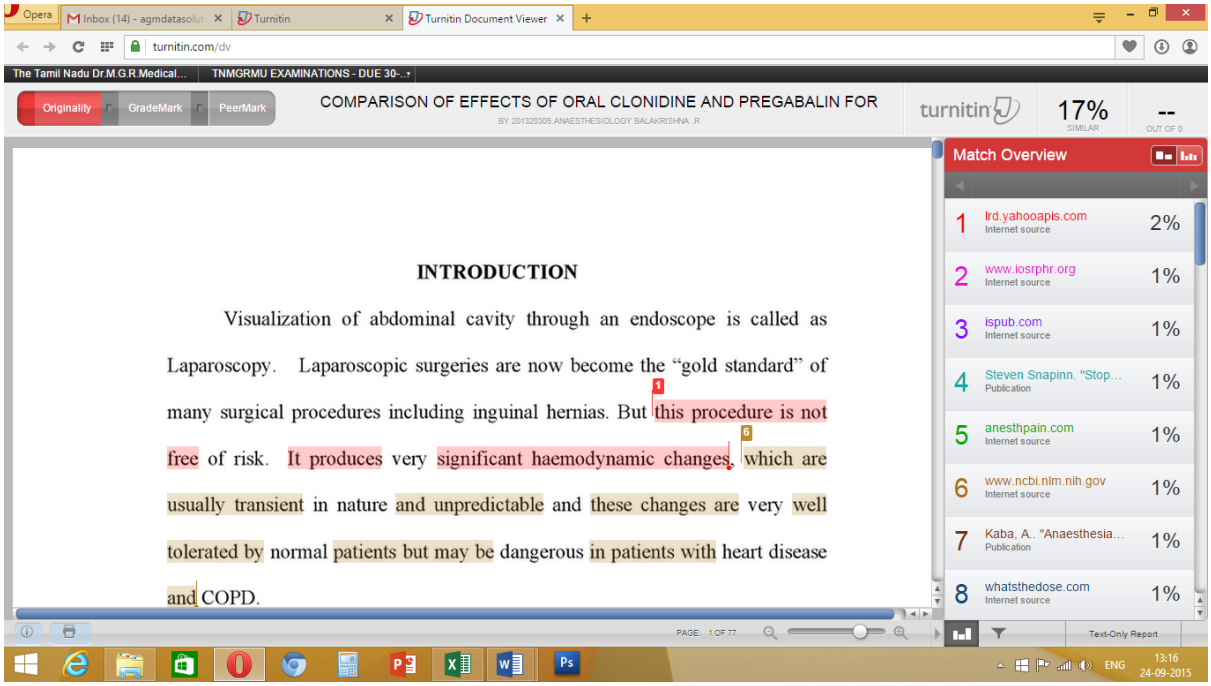
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INTRODUCTION
Visualization of abdominal cavity through an endoscope is called as Laparoscopy. Laparoscopic surgeries are now become the "gold standard" of many surgical procedures including inguinal hernias. But this procedure is not free of risk. It produces very significant haemodynamic changes, which are usually transient in nature and unpredictable and these changes are very well tolerated by normal patients but may be dangerous in patients with heart disease and COPD.
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ABSTRACT

Background:

Hemodynamic responses of laparoscopy should be attenuated by the appropriate premedication. The present study evaluated the clinical efficacy of oral premedication with Clonidine 200 µg or Pregabalin 150 mg for hemodynamic stability during laparoscopic surgeries.

Methods:

A total of 90 healthy adult patients aged 18 to 60 years with ASA physical status I & II of both gender, who met the inclusion criteria for elective laparoscopic surgeries, were randomized to receive Placebo Group I, Clonidine 200 µg Group II, or Pregabalin 150 mg, given 60 minutes before surgery as oral premedication. All groups were compared for heart rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure prior to premedication, before induction, after intubation 1 and 5 minutes, after pneumoperitoneum 1,5,15,30 & 45 minutes, after pneumoperitoneum release, and after extubation. Intraoperative analgesic requirement, post operative sedation ,pain scale and complications were also recorded.

Results:

Both Clonidine and pregabalin were effective in producing intra operative hemodynamic stability as compared to the control group by blunting the stress response

to pneumoperitonium but the hemodynamic stability is better with clonidine group than pregabalin group, which itself is better than placebo group.

The pain scores was significantly reduced in clonidine and pregabalin groups when compared to the placebo group but the reduction in scores in the pregabalin group is significantly less than that of the clonidine group.

The sedation score is higher in clonidine group when compared to placebo and pregabalin.

Intraoperative fentanyl requirement is more with placebo group than pregabaline group , which itself higher than clonidine group.

Drowsiness is more with clonidine group than pregabalin and placebo.

Post operative nausea and vomiting incidence was similar in all groups.

Conclusion:

This study concluded that oral premedication with Clonidine 200 µg and Pregabalin 150mg produces better hemodynamic stability in laparoscopic surgeries but Clonidine produces better haemodynamic stability than Pregabalin .Both drugs has significantly reduces intraoperative and post operative analgesic requirements without significant post operative respiratory depression.

Key words:

- Haemodynamic response, laparoscopic surgeries, Clonidine, pregabalin, Pneumaperitoneun,

INTRODUCTION

Visualization of abdominal cavity through an endoscope is called as Laparoscopy. Laparoscopic surgeries are now become the “gold standard” of many surgical procedures including inguinal hernias. But this procedure is not free of risk. It produces very significant haemodynamic changes, which are usually transient in nature and unpredictable and these changes are very well tolerated by normal patients but may be dangerous in patients with heart disease and COPD.

Pneumoperitoneum affects several homeostatic systems leading to alterations in cardiovascular, lung physiology and stress response.

The cardiac changes associated with pneumoperitoneum are an increasein mean arterial pressure reduction in cardiac output and increase in systemic vascular resistance which leads reduction in tissue perfusion.

Hence many drugs were used to prevent haemodynamic changes associated with pneumoperitoneum. To correct the reduction of cardiac output seen with raised pulmonary occlusion pressure and systemic vascular resistance Nitroglycerine was commonly used.

Clonidine helps in modulating the haemodynamic changes induced by pneumoperitoneum by inhibiting the release of catecholamine and vasopressin .

Pregabalin by binding to the calcium channels, modulates the release of several excitatory neurotransmitters like norepinephrine, substanceP, glutamate and calcitonin gene – related peptide.

The present study was designed to evaluate the extent of haemodynamic changes associated with laparoscopic surgery and also to compare the effects of oral Clonidine and Pregabalin in prevention of haemodynamic changes.

AIM AND OBJECTIVES OF THE STUDY

PRIMARY OBJECTIVE

To compare the effectiveness of oral Clonidine and oral Pregabalin for hemodynamic stability during laparoscopic surgeries.

SECONDARY OBJECTIVES

To determine

- The additional analgesic requirement
- The postoperative complications namely nausea, vomiting and drowsiness
- Post operative pain and sedation.

LAPAROSCOPIC SURGERY

Laparoscopic surgeries are very commonly done worldwide. Compared to an open procedure laparoscopy has many advantages like less surgical trauma, less stress response to operative procedure, less intraoperative and postoperative pain, early return of gastrointestinal function, better postoperative lung function and hence early discharge. For the patient minimal wound infection andabove all better cosmetic result.

The technique of laparoscopy involves insufflation of gas mostly carbondioxide into peritoneal cavity to separate the organs from abdominal wall by the creation of a pneumoperitonium. The gas insufflation is done by a specialised VERESS needle, at an initial rate of 2-4 lit /minute and pressure of 12-15 mm of Hg. Later the pneumoperitoneum is maintained by a gas flow at a constant rate of 200-400 ml/min.

Due to pneumoperitoneum intraoperative problems during laparoscopic surgery[1] can be cardiovascular, respiratory,renal, gastrointestinal or metabolic related. The main cardiovascular problems are decrease in venous return, reflex tachycardia and arrhythmias. Respiratory problems are due to cephalad displacement of diaphragm. It result in reduction of functional residual capacity, compliance by 30-50%. There is a rise in airway resistance in obese patients and persons with cardiopulmonary disease. Develpoment of atelectasis and intrapulmonary shunting leading to hypoxemia. Hypercarbia may also result from CO_2 absorption from pneumoperitonium. For this reason $ETCO_2$ (End tidal CO_2) monitoring is mandatory during laparoscopic surgeries.

Gastric regurgitation and aspiration are possible due to increased intra abdominal pressure. The instruments introduced into the abdomen may cause injuries to the visceral organs. Insertion of Trocharcan damage viscera; more likely a distended stomach usually by mask ventilation. Due to residual pneumoperitoneum there is increased incidence of nausea and vomiting after

laparoscopic procedure. Renal function and urine output are affected when the intra-abdominal pressure rises >20mmHg. Renal blood flow and glomerular filtration rate decreases as a result of increase in renal vascular resistance, reduction in glomerular filtration gradient and decrease in cardiac output. Other respiratory complications of gas insufflation are subcutaneous emphysema, pneumomediastinum, pneumopericardium, pneumothorax and venous gas embolism. In the preanaesthetic checkup, cardiac and respiratory function is assessed carefully. General anaesthesia with controlled ventilation[2] is the most common method. Ventilatory pattern is adjusted according to respiratory and hemodynamic response of the patient. Large tidal volumes (12-15ml/kg) prevent progressive microatelectasis and hypoxemia and allows for more effective alveolar ventilation and CO_2 elimination. However peak airway pressure is monitored to check excessive increase. Preferred volatile anaesthetic of choice is Isoflurane because it causes less myocardial depression and is less arrhythmogenic.

Pain consists of vague abdominal and shoulder discomfort while the Pain from trocharpuncture wounds are usually mild.

Hemodynamic Problems During Laparoscopy [1,3]

Hemodynamic changes during laparoscopy results as a consequence of pneumoperitoneum, hypercapnia, anaesthesia, and patient position. In addition there is a reflex increase of vagal tone and arrhythmias can also occur.

Peritoneal insufflation to IAP higher than 15 mm Hg induces significant hemodynamic alterations. These disturbances are characterized by fall in cardiac output, rise in arterial pressures and elevation of both systemic and pulmonary vascular resistances. Heart rate remains unchanged or increased only slightly. The decrease in cardiac output is proportional to the increase in IAP.

Cardiac output which decrease shortly after the beginning of the peritoneal insufflation, subsequently increase, probably as a result of surgical stress.

The mechanism of the decrease of cardiac output is multifactorial. Increased IAP results in venacaval compression, pooling of blood in the legs, and an increase in venous resistance.The decline in venous return, which parallels the decrease in cardiac output, is confirmed by a reduction in left ventricular end-diastolic volume measured using transesophageal echocardiography. Increase in cardiac filling pressures during peritoneal insufflation can be explained by the

increased intrathoracic pressure associated with pneumoperitoneum. During pneumoperitoneum, right atrial pressure and pulmonary artery occlusion pressure can not be considered as reliable indices of cardiac filling pressures. Abdominal insufflation interferes with venous return as suggested by the fact that atrial natriuretic peptide concentrations remain low despite increased pulmonary capillary occlusion pressure during pneumoperitoneum. By increasing circulating volume beforethe pneumoperitoneum can improve the venous return and cardiac output. Fluid loading or tilting the patient to a slight head-down position before peritoneal insufflations increases filling pressures.

Echocardiography studies have shown that the ejection fraction of the left ventricle, does not appear to decrease significantly when IAP increases to 15 mm Hg. However, all studies show an increase in systemic vascular resistance during the pneumoperitoneum.Although the normal heart tolerates rise in afterload within physiologic limits, the increases in afterloadproduced by pneumoperitoneum can be deleterious to patients with cardiopulmonary disease.

There is a relation between increase in systemic vascular resistance and patient position. The head-up position aggravates while the trendelenburg position attenuates the increase. By the administration of vasodilators like

nitroglycerin or nicardipine or volatile anesthetics like isoflurane, the increase in systemic vascular resistance can be corrected.

Both mechanical and neurohumoral factors raise the systemic vascular resistance. The involvement of neurohumoral factor is suggested by the gradual return of hemodynamic parameters to baseline values. In the presence of the pneumoperitoneum the levels of catecholamines, the renin-angiotensin system and especially vasopressin rises which increases the afterload. Peritoneal receptors are mechanically stimulated which results in increased vasopressin release, rise in systemic vascular resistance and arterial pressure. The rise in systemic vascular resistance also explains fall in cardiac output inspite of increase in arterial pressure.Use of centrally acting α_2-adrenergic agonist drugs like clonidine or dexmedetomidine and β-blocking agents like metoprolol drastically reduces hemodynamic changes and requirement of anaesthetic medications. Recent studies show the use of remifentanil in higher doses almost completely prevents the hemodynamic changes.

PHARMOCOLOGY OF CLONIDINE HYDROCHLORIDE[1,16]

Clonidine hydrochloride was introduced in early 1960s, as a nasal decongestant then its anti- hypertensive property was found out. Later on based on itspharmacological properties it is used in clinical anaesthesia.

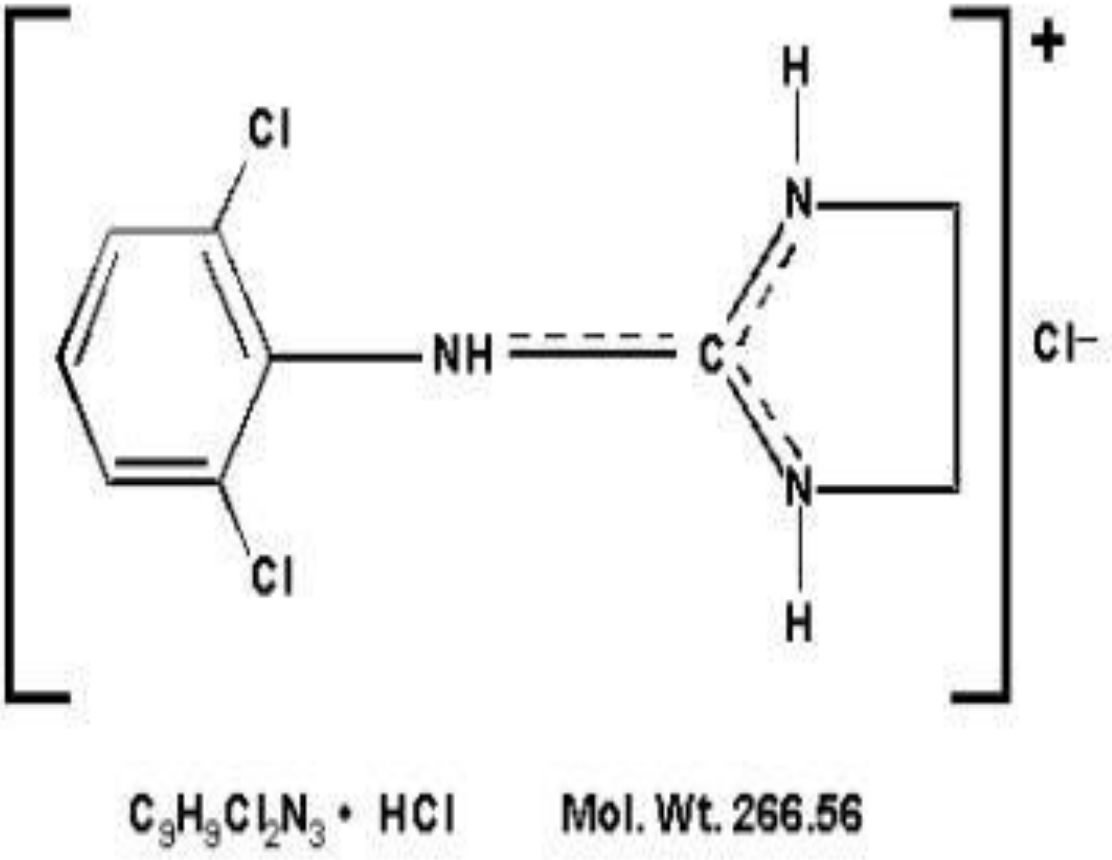


Figure 1. Clonidine Hydrochioride

Clonidine hydrochloride is an “imidazoline” compound and exists as a mesomeric compound. The chemical name : 2-(2, 6- dichlorophenylamino)-2imidazoline hydrochloride. The structural formula is “ $C_9H_9C_{12}N_3HCl$”.

The molecular wt is 266.56. Clonidine is an odourless, bitter, white, crystalline substance, soluble in both alcohol and water. Clonidine improves the quality of anaesthesia, provides intraoperative cardiovascular stability during surgery and decreases anaesthetic requirement. Clonidine may reduce the MAC value of volatile agents like halothane upto 50% in a dose dependent manner. In peripheral nerve blocks and central neuraxial blockade,Clonidine potentiatesthe anaesthetic action of the local anaesthetics with less side effects.

Availability:

Available as tablets in following strength:

100 microgram, 200 microgram and 300 micrograms.

Mechanism of action:

Clonidine is a centrally acting partial α_2 adrenergic agonist with a selectivity ratio of 220: 1 in favour of α_2 receptors. The α_2 receptors are of three subtypes:α_2a, α_2b, α_2c.

Sedation, analgesia and sympatholysis are mediated by α_2a receptors . α_2b receptors are responsible for vasoconstriction and anti- shivering. α_2c receptors are responsible for the startle response. Epidurally injected clonidine reaches the hypothalamus and medulla, by crossing the blood brain barrier as it is lipid soluble. It reduce the central neural transmission in the spinal neurons bystimulating the inhibitory $\alpha_2$adrenoreceptors.The analgesic effect is due to inhibition of substance- P release.

The α_2 adrenoreceptors are located on the afferent neurons in the superficial laminae of the spinal cord and in several brain stem nuclei implicated in analgesia. The superficial laminae contain 3 group of neurons :1. tonic,2. adapting, 3.single- spike firing.They receive their primary sensory input from Aδ and C fibres. Analgesic effect of clonidine due to the release of acetylcholine in the neuraxial region and inhibition of voltage gated Na^+ and K^+ channels which suppresses the generation of action potentials in tonic- firing spinal dorsal horn neurons. Sedation is due to its action on locus ceruleus.

Clonidine has opposing action at multiple sites after neuraxial or systemic administration .It therefore affects the systemic blood pressure in a complex manner. It reduces sympathetic drive by acting on the nucleus tractus solitarius and locus ceruleus of the brain stem through activation of post- synaptic α_2 adrenoreceptors. It also activates nor-adrenergic imidazoline preferring binding sites in the lateral reticular nucleus producing hypotension and anti-arrythmogenic action. In the periphery it acts on pre-synaptic α_2 adrenoreceptors at sympathetic terminals and decreases the release of nor-epinephrine causing vasorelaxation and reduced chronotropic drive. The brainstem and the peripheral effects of α_2 adrenoreceptor activation are counterbalanced by the direct peripheral vasoconstriction through its action on $\alpha_2$adrenoreceptors from the circulating concentrations of clonidine. The dose response curve for clonidine by neuraxial or systemic administration is U-shaped, with peripheral vasoconstriction from circulating drug concentrations at high doses opposing central sympatholysis.

Pharmacodynamics:

The analgesic effect of clonidine is more potent after neuraxial administration than systemicadministration.

Cardiovascular system:

Clonidine has minimal effects on responses to vasoconstrictors or anticholinergics given to treat hypotension or bradycardia respectively that may occur in neuraxial anaesthesia.

Sedation:

Clonidine produces sedation at the dose of 50 micrograms or more in less than 20 minutes. Sedation is dose dependent and irrespective of the route of administration.

Respiration:

Clonidine doesn’t produce respiratory depression even after massive overdose.They do not potentiate respiratory depression from opioids.

Peripheral nerves:

At high concentrations a minor degree of blockade is noted with some preference for C- fibres in the peripheral nerves. It therefore enhance the peripheral nerve block when added with local anaesthetics due to the absence of $\alpha_2$adrenoreceptors on the axons of peripheral nerves.

Pharmacokinetics:

Oral Clonidine has nearly 90% bio availability because of its good oral absorption. The mean half-life of the drug in plasma is about 10 - 12 hours. 70% of drug is excreted in an unchanged form by the kidney, and its half- life increases in renal failure and hence dose adjustment to be done.

In transdermal route drug is released at a constant rate for a week. Steady state concentration achieved by 72 hours.

Because of its high lipid solubility, it rapidly distributes into extra- vascular sites including the central nervous system.

Distribution t ½	:	11 ± 9 minutes.
Elimination t½	:	9 ± 2 hour, 41 hours in severe renal dysfunction.
Volume of distribution	:	2.1 ± 0.4 l/kg
Plasma protein binding	:	22 - 40%.
Metabolism	:	Minor pathways with the major metabolite is P- OH clonidine

Excretion:

70% of the dose, mainly in the form of unchanged parent drug in urine. So, the elimination t½ of clonidine varies as a function of creatinine clearance. In subjects undergoing hemodialysis only 5% of the body clonidine store was removed.

Adverse effects:

1. General**:** Weakness, fatigue, headache and withdrawal syndrome, pallor.

2. Cardiovascular: palpitations, tachycardia, bradycardia about 5 in 1000 syncope, raynaud's phenomenon, congestive cardiac failure, ECG abnormalities like sinus node arrest, junctional rhythm, AV block and arrhythmias are reported.

3. Central nervous system: nervousness, agitation, mental depression, insomnia, vivid dreams or night mares.

4. Dermatological: rash, angioneurotic edema, pruritus, urticaria and alopecia.

5. Gastro intestinal tract: nausea and vomiting, anorexia, malaise, transient abnormalities in liver function tests, hepatitis.

6. Genitourinary: in chronic intake leads to decreased sexual activity, impotence, loss of libido, nocturia.

7. Hematologic: thrombocytopenia rarely.

8. Metabolic: weight gain and gynaecomastia

9. Musculoskeletal: muscle pain, joint pain and leg cramps.

10. Ear, nose and throat: Nasal mucosa dryness.

11. Opthalmological: dryness, burning of eyes.

Precautions:

1. In renal insufficiency patient , dose reduction needed.

2. Sudden withdrawal produces hypertensive crisis. So it should be gradually discontinued over 2 to 4 days.

3. Use with caution in patients with cerebrovascular or coronary insufficiency.

4. Intrathecal / epidural clonidine often causes bradycardia that if symptomatic can be treated with inj. Atropine.

Contraindications:

1. History of hypersensitivity to clonidine or its components.

2. In patients with bradyarrhythmia or AV block.

3. Patients with severe cardiovascular disease

4. Patients with cardiovascular / hemodynamic instability.

Interactions:

1. Clonidine potentiates the CNS- depressant drugs like alcohol, barbiturates and other sedatives.

2. Narcotics potentiate the hypotensive effects of clonidine,
   While tricyclic anti depressants antagonize hypotensive effects.

3. Co-administration of drugs with a negative chronotropic drugs such as beta blockers, digoxin can potentiate bradycardiac rhythm disturbances.

4. Beta blockers may potentiate the hypertensive responses produced by clonidine withdrawal.

Indications:

1. To prolong the duration of epidural/ spinal anaesthesia and Peripheral nerve block.

2. As adjuvant for the treatment of intra operative and post operative pain.

3. In epidural add on agent for relief of severe cancer pain.

4. As an anxiolytic.

5. For sedation.

6. To prevent or treat per operative shivering.

Anaesthetic uses:

1. Premedication: By acting on locus ceruleus in central nervous system produces sedation. Also got an anaesthesia- sparing effect.

2. Hemodynamics: Prevents hypertension and tachycardia during laryngoscopy and intubation as well as during surgical stimulation.In cardiac and vascular sugeries it reduces the incidence of myocardial ischemia.

3. Epidural:As a sole agent or in combination with opioids or local anaesthetics it provides excellent analgesia in labour analgesia.

4. Spinal: Clonidine along with local anaesthetics improves the quality of analgesia and duration of block.It minimize the tourniquet pain during limb surgeries, and prevents shivering.

5. Caudal: With local anaesthetics increases the duration of caudal anaesthesia and analgesia by 2 or 3 times without hemodynamic side effects. Dose 2-3 mics/kg

6. Peripheral nerve blocks: prolongs the duration of block and analgesia with local anaesthetics by 2 times in a dose of 75 to150 micro grams.

7. Bier's block: Enhances the tolerance of tourniquet.

8. Intra articular analgesia.

Overdosage and treatment:

There is no specific antidote for clonidine overdosage. Supportive measures like atropine, ephedrine, i.v fluids is enough.

For hypertensive crisis Inj.phentolamine, i.v furosemide, diazoxide can be used.

Yohimbine partially reverses sedation and analgesia but not BP and heart rate changes produced by epidurally injected clonidine.

Opioid antagonist Naloxone used as an adjunct for management of clonidine induced respiratory depression, hypotension and or coma. Blood pressure monitoring is essential after injecting naloxone because it produces paradoxical hypertension

PHARMACOLOGY OF PREGABALIN[16]

Pregabalin is a structural analog of Gamma amino butyric acid and acts by presynaptic binding to the α-2 delta subunit of the voltage gated calcium channel.These channels are widely distributed in brain and the spinal cord.

By binding to the calcium channels, pregabalin modulates the release of several excitatory neurotransmitters like noradrenaline, glutamate, substanceP, and calcitonin gene – related peptide. This leads to inhibitory modulation of "overexcited neurons" and returns them back to their "normal" state.

Pregabalin reduces Tissue damage induced hyperexcitability of dorsal horn neurons .

Pregabalin has a more appropriate pharmacological profile than gabapentin including dose dependent absorption and more potent than gabapentin at the same time producing fewer side effects

Pregabalin belongs to gabapentenoid group of drugs. It possesses chemical structure similar to inhibitory neurotransmitter gamma amino benzoic acid. Pregabalin has got similar properties like the prototype drug gabapentin.

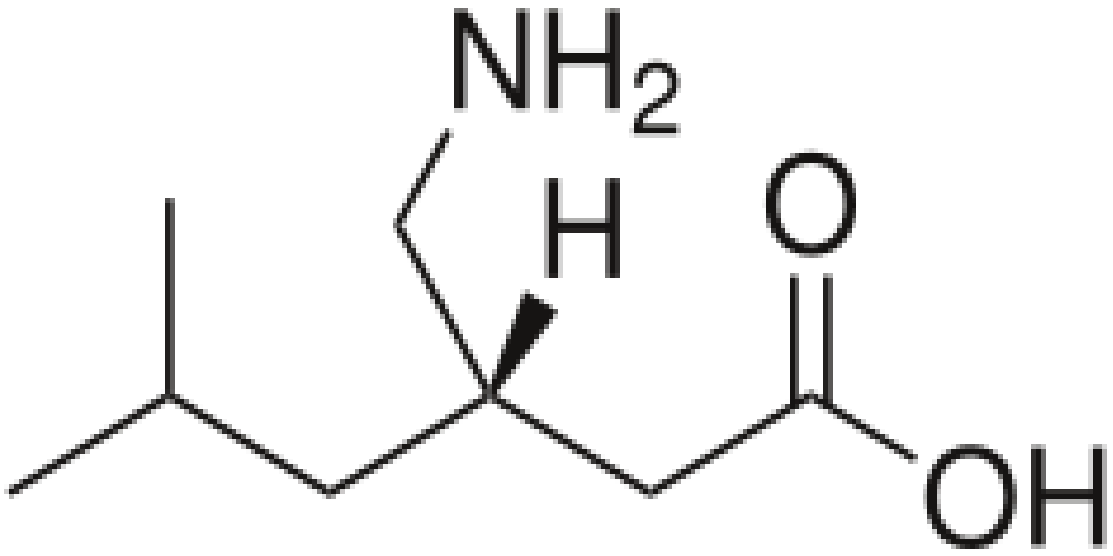


Figure 2. Pregabalin

Chemical structure of Pregabalin

Pregabalin which is chemically S-(+)-3-isobutylgaba (Fig-1), was designed as a lipophilic analogue of GABA (gamma-amino butyric acid) substituted at the 3-position to facilitate diffusion across blood brain barrier.3-isobutylgaba exists in isomeric forms, rendering the drug pharmacologically active enantiomer.

Drug approval

- In Europe during july 2004 first granted the Pfizer company approval for pregabalin, for the treatment of peripheral neuropathy and partial seizures.
- December 2004-The888888 Food and Drug Administration (FDA) approved pregabalin, for the treatment of diabetic peripheral neuropathy and post herpetic neuralgia.
- The FDA approved pregabalin for use as an adjuvant in partial seizure treatment in june 2005.
- March 2006- Pregabalin got approval from European commission, for the treatment of generalised anxiety disorder.

Mechanism of action:

Pregabalin has structural similarity to the inhibitory neurotransmitter GABA. It neither acts on GABA receptor, nor mimics it physiologically. The exact mechanism of action of pregabalin has not been fully known. Pregabalin has pharmacological profile similar to gabapentin. Pregabalin acts on the alpha 2 delta subunit of neuronal calcium channels.

Pregabalin is an alpha 2 delta ligand

Alpha 2 delta is a subunit of presynaptic, voltage-gated calcium channel. The main site of action of pregabalin is alpha 2 delta subunit of neuronal calcium channels. Binding to this ligand reduces the depolarisation induced calcium entry at nerve terminals which leads to decrease in the release of excitatory amino acids like glutamate, noradrenaline, substance-P, and CGRP. This modulation ofneurotransmitter release by pregabalin is responsible for its anxiolytic, anticonvulsant and analgesic properties.

There are 6 types of Voltage gated calcium channels namely P, Q, N, L, R, and T-type channels. N-type calcium channels are responsible for pain sensitization phenomenon in response to noxious stimuli. Calcium channel blockers binds to L-type calcium channels. L- type calcium channels are present in Cardiac and other peripheral tissues. This explains the lack of cardiovascular side effects with pregabalin.

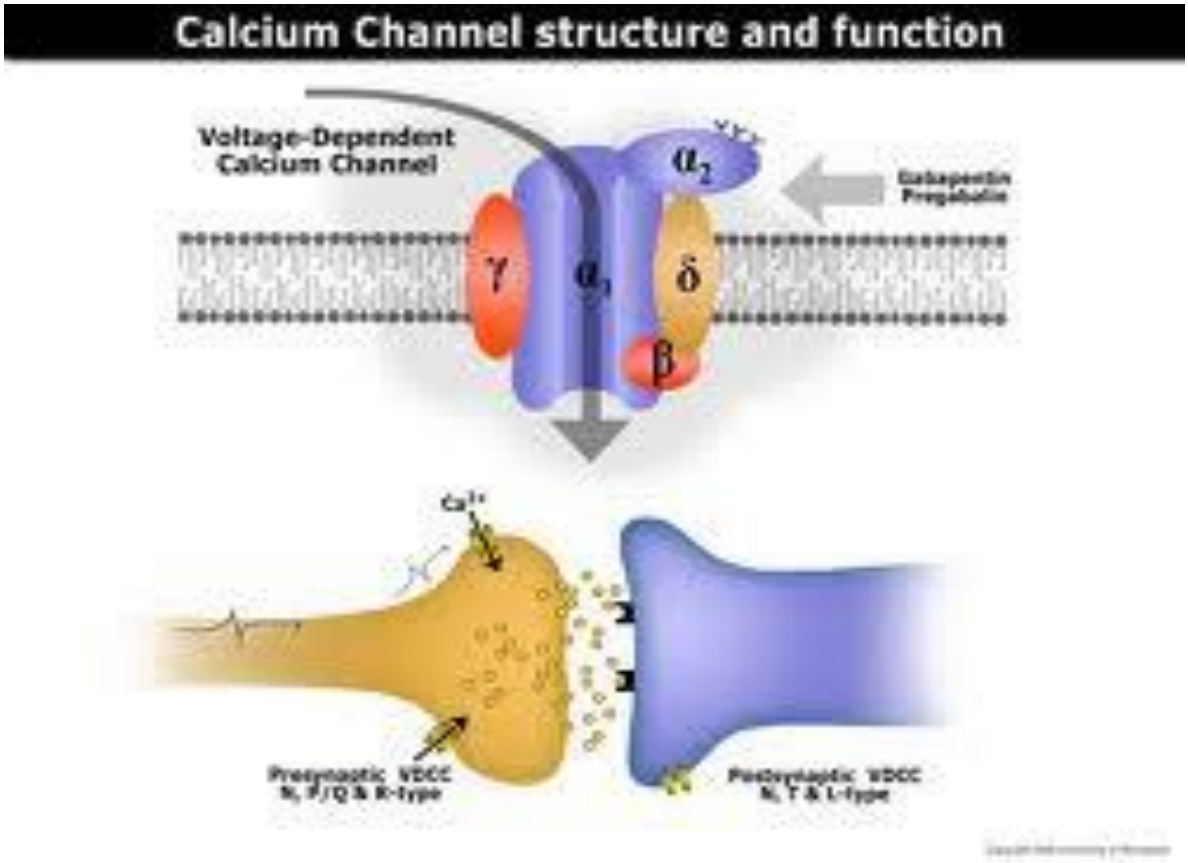


Figure 3. Structure of calcium channel

Dosage and administration:

The maximum recommended dosage for painful diabetic neuropathy is 100 mg three times a day. The dose needs to be reduced in patients with reduced renal function since pregabalin eliminated via renal route. For peripheral neuropathy, start with low doses 75 mg per day and may be increased to 300 mg per day within a 7 days based on efficacy and patient tolerability.

PHARMACOKINETICS

Pregabalin has consistent dose proportional pharmacokinetics

The mean elimination half-life of pregabalin is 6.3 hours, which is independent of dose and repeated administration. This consistent dose-proportional pharmacokinetics of pregabalin provides confidence in the prediction of dose-response relationship in clinical practice. Administration of pregabalinalong with food has no effect on its absorption.

Distribution, metabolism and elimination

L-transporter system is responsible for transport of substances across the brain and gut. Pregabalin is a substrate of this L-transporter system so it crosses

blood brain barrier very rapidly. This property is essential for a drugs acting on central nervous system.

Pregabalin undergoes less than 2% metabolism. It is usually excreted via kidney in unchanged form. In renal failure patients dose reduction needed. 50% dose reduction needed in patients with creatinine clearance of 30 to 60 ml/minute.

Pregabalin versus gabapentin

As discussed earlier pregabalin has better pharmacokinetic properties than gabapentin although both belongs to same group and have similar chemical structure.

Table 1.Pharmacological properties of pregabalin

Property	Clinical significance
1. High affinity for α2δ receptor	New mechanism of action
2. No effect on GABA	No retinal or optic nerve toxicity
3. Linear dose proportional to Cmax	Predictable level and dose response
4. Lack of protein binding	No drug interactions
5. Negligible metabolism	No drug interactions
6. Renal excretion (98% unchanged)	Dose reduction in renal impairment
	No hepatic effects
7. Rapidly cross blood brain barrier	Access to CNS site of action

Cmax- maximum plasma concentration

Pregabalin lacks drug interactions:

Pregabalin does not affect the liver cytochrome P450 enzyme system and it does not bind to plasma proteins and hence has no drug interactions. So it can be safely administered with other medications including anticonvulsant.

Safety implications of pregabalin:

Pregabalin even at high concentration does not completely block calcium channel function or transmitter release and hence no complication occurs in drug overdose.

Clinical uses of pregabalin

1. Adjuvant drug in partial seizures
2. Chronic pain syndromes like diabetic peripheral neuropathy and post herpetic neuralgia.
3. Chronic anxiety disorder
4. Adjuvant in acute pain management

Pregabalin has anticonvulsant, sedative, analgesic and anti-hyperalgesic properties studies and are used for pre-operative sedation, anxiolysis, reduced inter-operative opioid requirement and attenuation of hemodynamic stress response to laryngoscopy and tracheal intubation.

Alpha 2 delta receptors are involved in the mechanism of neuronal hypersensitisation to noxious stimuli.Pregabalin blunts this hypersensitisation and helps in reducing the post-operative pain and has got opioid sparing effect.

Side effects and precautions:

Pregabalin is a relatively safe drug; well-tolerated with dose-dependent adverse effects usually mild and transient which includes

1. Dizziness (29%)
2. Somnolence (22%)
3. Dryness of mouth (9.1%)
4. Blurred vision (6.4%)
5. Edema (6.1%)
6. Weight gain (5.6%)
7. Abnormal thoughts (5.4%)

Pregabalin is contraindicated in patients with history of drug allergy. FDA approval for pregabalin is in class C for pregnant patients.

REVIEW OF LITERATURE

A number of clinical studies have been undertaken in the past to assess the efficacy of clonidine and pregabalin on haemodynamic changes.

Kumkum gupta et al[4] in 2011 analysed "oral premedication with pregabalin or clonidine for hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy comparative evaluation methods laparoscopic patients randomised to receive placebo Group I, pregabalin (150mg) Group II and clonidine (200microgram) Group III given 75 to 90 mins before surgery as oral premedication. Concluded that oral premedication with pregabalin or clonidine causes sedation and anxiolysis with hemodynamic stability during laryngoscopy and laparoscopic cholecystectomy", without prolongation of recovery time and side effects.

In Yuvesh Passi et al [5] analysed " fifty patients belonging to ASA status I or II, posted for laparoscopic Cholecystectomy were selected and randomly allocated to two groups A & B. Group A (clonidine) received Tab. clonidine 150µg orally and Group B (Control) received Tab. vitamin B complex orally as premedication 60-90 minutes before laparoscopy. Heart rate and mean blood pressure were recorded prior to intubation, 15 min after intubation, at skin incision, 15 min and 30 min after pneumoperitoneum and 15 min after pneumoperitoneum release. Concluded that premedication with oral tablet

clonidine 150 μg provides stable hemodynamics in laparoscopic cholecystectomy" patients.

Malek et al[6] in 1999 analysed in their work involving 21 patients the incidence of these effects and tried to suppress them by premedication with clonidine. 21 patients were given 0.15 mg clonidine in an infusion 15 minutes before operation and 21patients were given 0.15 mg clonidine by the i.m. route 60-90 mins before operation. A highly significant drop in the incidenceof hypertension was recorded during operation for systolic pressure ($p < 0.001$) after both ways of administration, as well as of diastolic pressure ($p < 0.01$ for intravenous and $p < 0.05$ for intramuscular premedication). Premedication with intravenous clonidine can be recommended as a routine procedure before laparoscopic cholecystectomies.

Yu et al[7] in 2003 analysed " thirty-two patients scheduled for elective laparoscopic cholecystectomy were recruited for a prospective, randomized, double-blinded comparative study. They were allotted randomly to two groups: Placebo and clonidine. Patients in the placebo group ($n = 16$) were premedicated with oral antacid, while those in the clonidine group ($n = 16$) were premedicated with oral clonidine 150 μg before anesthesia. Analysis of heart rate variability was used to quantify the control of heart rate at baseline, and during the pneumoperitoneum and recovery periods. Time of the first request for postoperative analgesic and cumulative analgesic requirements in 24 h were

recorded. Concluded that Clonidine preserves heart rate control in pneumoperitoneum and recovery periods". Oral clonidine premedication reduces the postoperative analgesia requirement.

Mrinmoy et al[8] in 2007 analysed "sixty patients of ASA I & II, posted for elective laparoscopic cholecystectomy were recruited for a prospective randomized, double-blinded comparative study. They were randomly allocated into two groups to receive either oral clonidine 150 µg (Group C) or ranitidine 150 mg (Group P) 90 minutes before surgery. Significant increase in heart rate was noted after pneumoperitoneum in Group P as compared to Group C. Similarly, rise in systolic arterial pressure, diastolic arterial pressure and mean arterial pressure was more in Group P following pneumoperitoneum. Incidence of PONV and shivering was also less in Group C. Concluded that clonidine premedication provides better haemodynamic stability", so it can be recommended as a routine premedication for laparoscopic procedures.

In Masayoshi uchida et al[9] studied in 2004, sixty patients of ASA I were randomly allocated into two groups. Thirty patients received tab. famotidine 20 mg (control group) orally 90 min before the induction, the remaining 30 patients received clonidine 5 µg/kg and famotidine 20 mg (clonidine group). MAP, CI and HR responses to hypercapnia in the clonidinel group were significantly attenuated compared with control group. Plasma norepinephrine concentrations were significantly lower in clonidine group.

In Laisalmi et al[10] study in 2001; The “effects of clonidine 4.5 mg/kg or saline on hemodynamics, neuroendocrine response and renal parameters were compared in 30 healthy patients undergoing laparoscopic cholecystectomy.Heart rate, arterial blood pressures and plasma renin activity were lower during and after pneumoperitoneum in patients with clonidine. There were no differences in urine output, urine oxygen tension (reflecting medullary perfusion), or antidiuretic hormone between the groups. N-acetyl-b-D-glucosaminidase, a marker of proximal tubular damage, was minimally elevated after clonidine. Concluded that clonidine enabled stable hemodynamics” and prevented activation of RAAS seen as unchanged plasma renin activity.

In Sung et al[11] study; “One hundred and ten patients scheduled for elective laparoscopic cholecystectomy were randomly allotted to either of the placebo or clonidine group. Patients of the placebo group (n = 65) were premedicated with oral antacid (300 mg), while those in the clonidine group (n = 45) were premedicated with oral clonidine 150 micrograms prior to anesthesia. The premedication was given 60 to 90 min before the anticipated time of induction of anesthesia. Concluded that oral clonidine premedication helped to provide perioperative hemodynamic stability, spared the use of isoflurane and reduced the requirement of postoperative analgesia so as to smoother the way to recovery in patients undergoing laparoscopic cholecystectomy”.

Jokela R et al[12] conducted a “randomized control trial of perioperative administration of pregabalin for pain after laparascopic hysterectomy. In this study they evaluated the control of pain after perioperative administration of pregabalin 300 or 600 mg. 91 patients scheduled for laparascopic hysterectomy were randomized to receive either diazepam 10mg, pregabalin 150mg or pregabalin 600 mg as premedication and the dose was repeated after 12 hours except the diazepam group where they received placebo. Until the first postoperative morning analgesia was provided by oxycodone using patient controlled analgesia. This study concluded that perioperative administration of pregabalin 600mg decreases oxycodone consumption compared with diazepam 10mg” but is associated with an increased incidence of side effects.

Dinesh k et al[13] in march 2015 analysis done on comparative study of oral pregabalin 150 mg and clonidine 200 microgram for attenuation of haemodynamic responses to laryngoscopy and tracheal intubation. Concluded that both pregabalin and clonidine successfully attenuated the hemodynamic response to laryngoscopy and tracheal intubation. Pregabalin better attenuates pressor response and clonidine better attenuates tachycardia response.

Balaban F et al[14] analysed the efficacy of two different doses of preoperative pregabalin (150 mg and 300 mg) on pain relief and total opiod consumption after laparascopic cholecystectomy. The results of this study showed that preemptive pregabalin decreased pain scores and postoperative

fentanyl requirement in patients undergoing laparascopic cholecystectomy in a dose dependent manner. There was also no difference in side effects between two different groups on two different dosages.

George RB et al[15] performed a study to determine if low dose of pregabalin could decrease opioid use following abdominal hysterectomy while comparing placebo. Patients were randomised into three groups- pregabalin 75 mg(P75), pregabalin 150 mg(P150) and placebo. The study drug was administered two hours prior to surgery and 12 hour following the initial dose. Postoperative pain was managed using patient controlled analgesia with morphine. Pain at rest and movement as well as nausea were assessed. Mean cumulative morphine consumptionwas noted postoperatively. This clinical trial showed pregabalin treatment may not be use in reducing opioid use upto 24 hour postoperatively.

METHODOLOGY

SOURCES OF DATA

Data was collected from 90 ASA I and II patients scheduled for laparoscopic surgeries aged between 18 – 60 years at Tirunelveli Medical College and Hospital,Tirunelveli. Both study groups and control were selected from these patients. The study was conducted over a period of four months.

INCLUSION CRITERIA :

- ASA I and II patients
- Both gender
- Age 18 -60yrs

EXCLUSION CRITERIA

- Pre-existing cardiac disease
- Known case of Systemic Hypertension
- Renal ysfunction
- Hepatic dysfunction
- Anticipated difficult intubation

- Patient refusal

- Allergic to any of the study drugs

METHODS

The study was a prospective, randomized placebo control study. Computer based randomization was done.

MATERIALS

Clonidine tablet 200µg

Pregabalin tablet 150mg

Placebo tablets

Drugs- Injection Midazolam, Injection Glycopyrrolate, Inj Fentanyl, Inj.propofol, Inj. Vecuronium, Inj. Neostigmine, Isoflurane, emergency drugs, Normal Saline and Ringer Lactate.

Monitors- ECG, NIBP, SPO2, EtCo2.

Study design:

The patients satisfying inclusion criteria were randomly allocated into three groups each containing 30 patients.

Preanaesthetic evaluation:

1. History

2. Clinical examination

3. Relevant investigations

4. Informed consent from patients

Preanaesthetic medication was given with tab.ranitidine 150 mg and tab.diazepam 10 mg the night before surgery. Patients were randomly allocated into three groups.

1) Group I– Those who receive placebo tablets.

2) Group II - Those who receive Clonidine tablets (200 µg)

3) Group III - Those who receive Pregabalin tablets (150 mg)

The tablets given orally with sips of water 60 mins before induction of general anesthesia. Before administration of oral premedication , each patients baseline heart rate, systemic blood pressure, diastolic blood pressure and mean arterial pressure and SpO_2 recorded.

After shifting the patient to the operation table SpO_2, NIBP, ECG monitors were attached. The baseline values were recorded. IV access was established. Inj.midazolam 0.03mg/kg and inj.glycopyrrolate 0.2 mg i.v. given and patient pre-oxygenated for 3 minutes. Anesthesia was induced with inj.propofol 2mg/kg, inj.fentanyl 2 microgram/kg and inj.vecuronium 0.1 mg/kg. Proper size cuffed PVC endotracheal tube was inserted orotracheally. Anaesthesia was maintained with NitrousOxide 67%, Oxygen 33% ,isoflurane 1% and intermittent doses of inj.vecuronium and inj.fentanyl. Ventilation was controlled mechanically and was adjusted to keep $ETCO_2$ between 30 to 35 mm of Hg. The intra abdominal CO_2 pressure was kept between 12 -14 mm of Hg. A ryles tube was inserted and suction applied to empty the contents of stomach after intubation and also before extubation.

Haemodynamic instability was defined as "Heart rate and blood pressure fall or rise more than 15% from baseline" and was treated accordingly. Systemic arterial pressure including the systolic, diastolic and mean arterial pressure, heart rate, SpO_2 were recorded as

(1) Pre operative (pre op)

(2) One minute after endotracheal intubation (AI 1 MIN)

(3) Five minutes after endotracheal intubation (AI 5 MIN)

(4) One minute after pneumoperitoneum (AP 1 MIN)

(5) Five minutes after pneumoperitoneum (AP 5 MIN)

(6) Fifteen minutes after pneumoperitoneum (AP 15 MIN)

(7) Thirty minutes after pneumoperitoneum (AP 30 MIN)

(8) Fourtyfive minutes after pneumoperitoneum (AP 45 MIN)

(9) After pneumoperitoneum release (PR)

(10) After extubation (AE)

Reversal of muscle relaxation was done with inj.glycopyrolate 0.01 mg/kg body weight and inj.neostigmine 0.05 mg /kg and patient was extubated.

Postoperatively all episodes of PONV and drowsiness experienced by the patient during the first 6 hours after anaesthesia was recorded. Rescue Antiemetic (inj.ondansetron 4mg) was used if patient had nausea or vomiting and the number of doses required was monitored. Post operative pain and

sedation of the patient was monitored for 6 hours using the visualanalog scale and the ramsay sedation score respectively.

Pain quantification was done on a modified Visual Analog Scale Score between 0 and 10 (0 = no pain to 10 = worst imaginable pain.

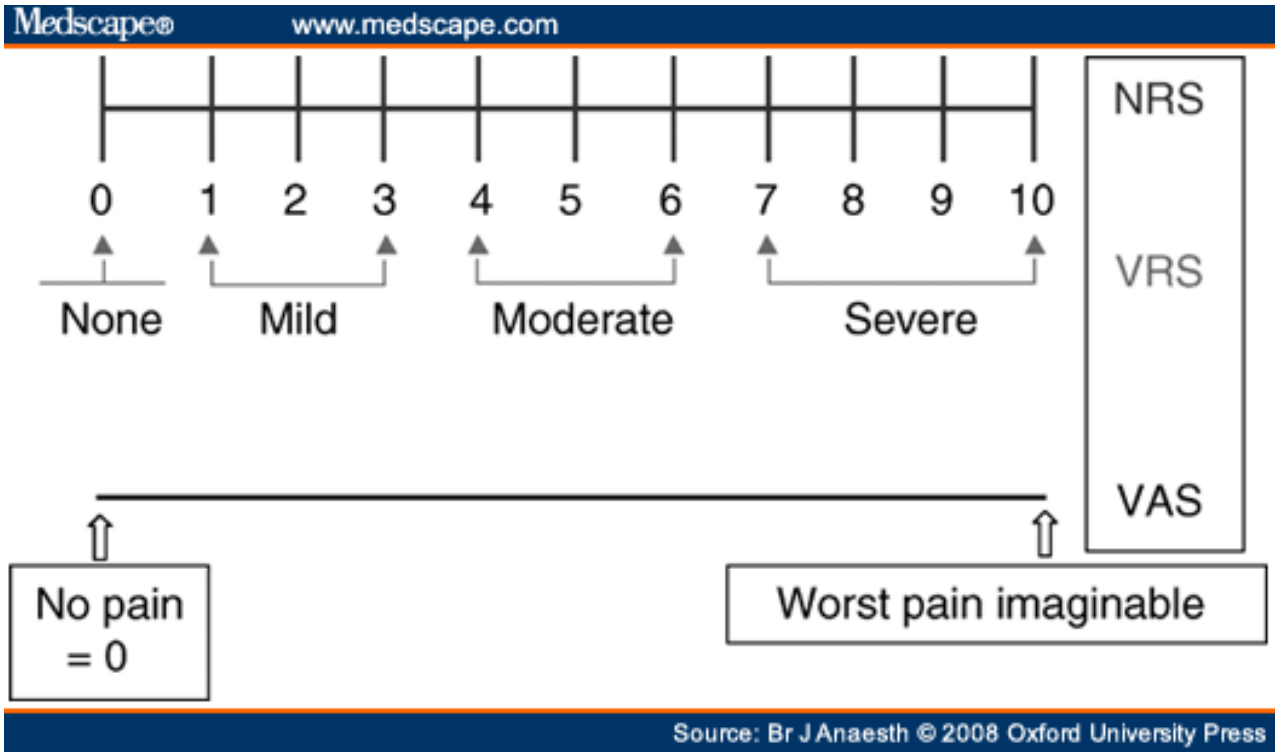


Figure 4.Visual Analog Scale Scoring

RAMSAY SEDATION SCORE

LEVELS 1 -3 patient awake

Level 1-anxious and agitated or restless or both

Level 2-cooperative and oriented

Level 3-responds to commands only

LEVEL 4-6 patient asleep, responds to light glabellar tap or loud auditory stimulus

Level 4 –Brisk response

Level 5 – Sluggish response

Level 6 –No response

The pain scores, sedation scores were recorded preoperatively, after extubation then at 1, 2, 4 and 6 hours.

Statistical Methods

Information collected regarding all the selected cases were recorded in a Master Chart. The statistical analysis was done using SPSS statistics software version.

A 'p' value less than 0.05 is taken to denote significant relationship.

RESULTS

DEMOGRAPHIC PROFILES

The three groups were comparable in characteristics like age, sex, ASA and baseline parameters.

Table 2.Relationship between the demographic variables and other variables.

Demographic profile	**Group1 (Mean±SD)**	**Group 2 (Mean±SD)**	**Group3 (Mean± SD)**	**P value**
AGE	44.763±6.972	44.1±8.623	45.6±7.892	0.11
SEX	14:24	12:18	12:18	0.545
ASA	22:16	16:14	15:15	0.778
HR	77.815±5.765	82.2±4.759	78.3±6.539	0.511
SBP	124.81±10.88	121.266±9.860	121.7±9.804	0.222
DBP	77.394±7.027	75.933±8.901	78±7.1798	0.06
MAP	92.947±7.738	90.3±8.0693	92.2±7.344	0.088
DURATION	54.166±5.736	53.333±6.0647	53.2±5.865	0.81

Inference

Since the p value is greater than 0.05, there is no significant relationship between the group 1,2 and 3 in terms of age,sex, ASA, duration, Baseline HR, SBP, DBP

and MAP.

Figure 5.Relationship between the demographic variables and other variables.

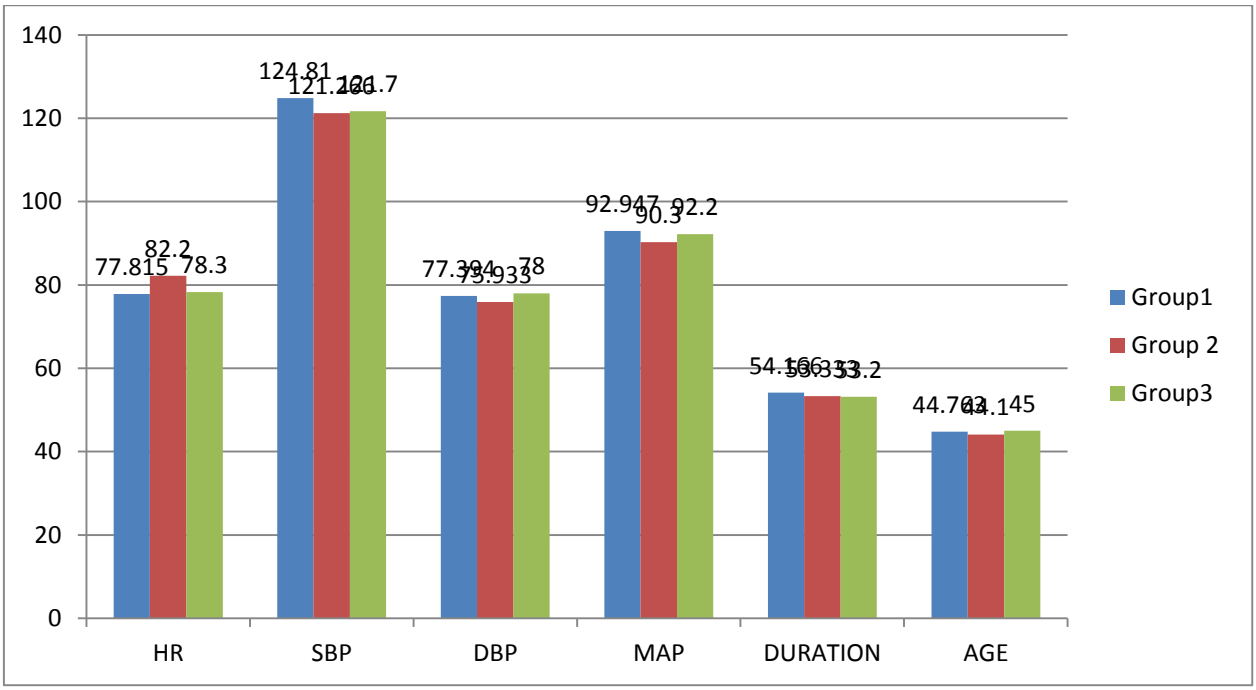


Figure 6.Relationship between the gender distribution.

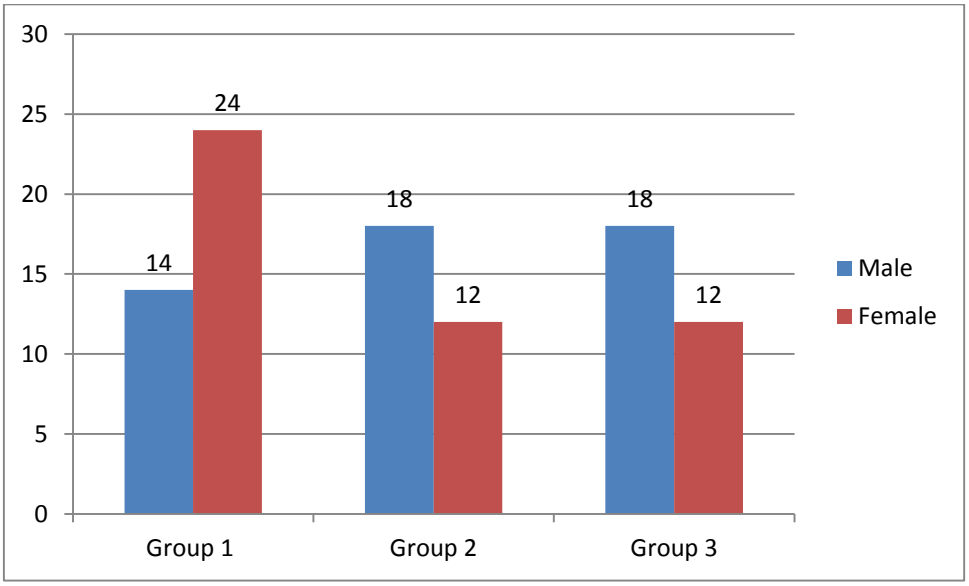


Figure 7.Comparison of ASA status

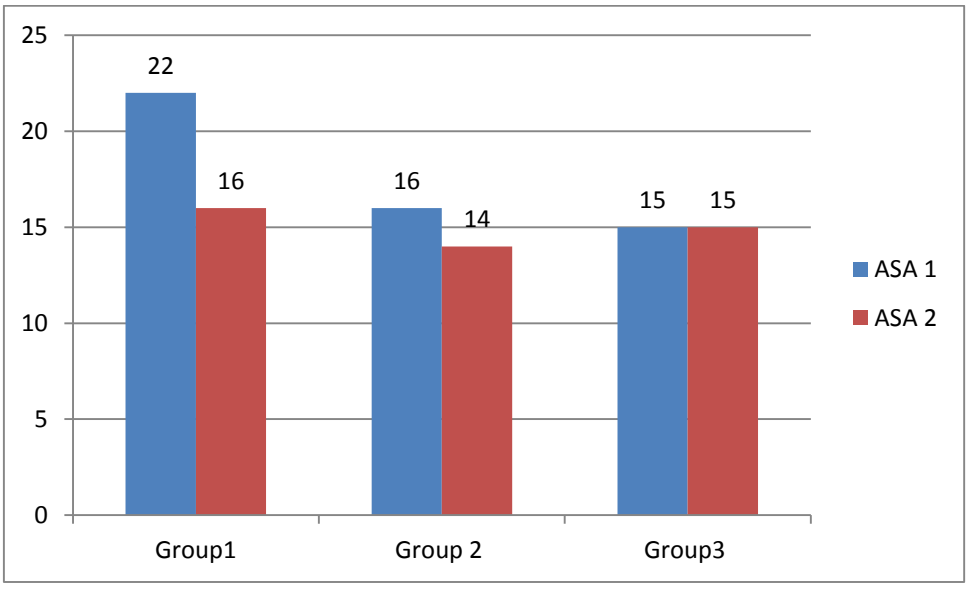


Figure 8. Comparisonbetween baseline parameters.

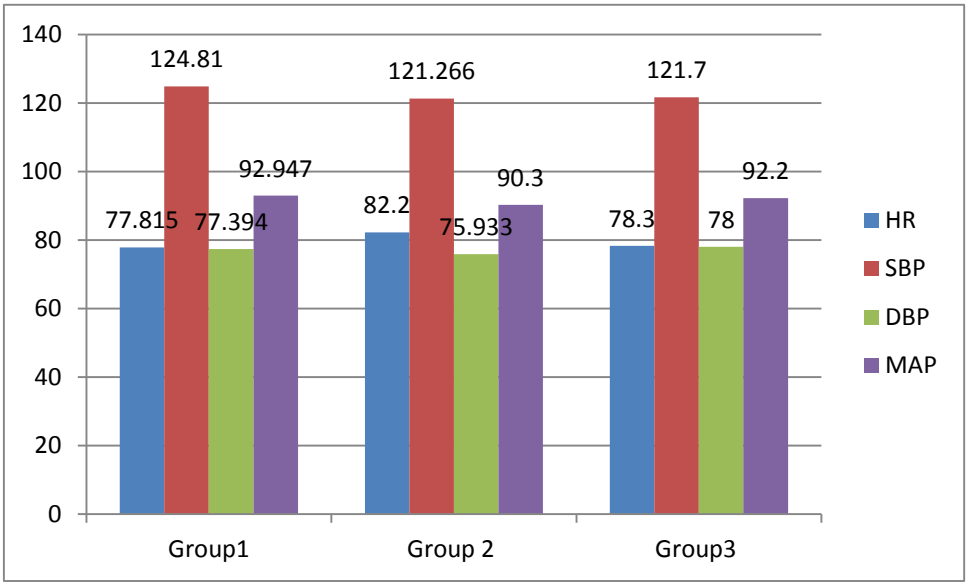


Table 3.comparingHR, SBP, DBP, MAP in group 1,2 and 3

GROUP	1 **(Mean±SD)**	2 **(Mean±SD)**	3 **(Mean±SD)**	p-value
HR preop	81.39±5.091	77.13±5.734	79.9±5.845	0.008
HR AI 1min	91.08±8.423	79.63±5.786	84.83±6.502	0
HR AI 5min	88.6±4.868	77.67±6.11	82.23±5.557	0.08
HR AP 1min	99.26±9.83	82.4±6.134	91.37±7.937	0
HR AP 5min	93.79±11.989	80.53±6.852	92.37±7.591	0
HR AP 15min	95.57±9.676	80.93±6.512	93.9±7.053	0
HR AP 30min	92.95±7.763	78.13±6.986	86.5±7.243	0
HR AP 45min	89.05±5.337	77.1±7.029	87.4±7.025	0
HR PR	84.95±4.893	74.3±6.587	83.8±3.978	0.772
HR AE	77.39±36.403	79.33±4.656	74.43±30.978	0.005
SBP preop	123.68±9.779	118.47±9.475	119.83±9.158	0.006
SBP AI 1min	148.97±16.747	116.87±11.443	124.87±12.719	0
SBP AI 5min	130.73±9.27	114.83±10.596	118.03±10.833	0.81
SBP AP 1min	147.34±13.921	124.3±9.444	121.3±14.089	0
SBP AP 5min	142.74±16.003	123.4±8.439	128.93±14.225	0
SBP AP 15min	146.97±10.545	123.9±7.522	128.9±13.33	0
SBP AP 30min	134.37±16.534	124.2±8.556	128.07±14.701	0.012

SBP AP 45min	130.61±13.962	122.67±8.727	125.27±14.946	0.039
SBP PR	111.92±1.075	101.1±15.302	111.8±1.375	0.661
SBP AE	116.21±1.473	111.37±0.964	115.1±1.296	0
DBP preop	77.82±6.939	76.8±9.155	76.97±6.636	0.024
DBP AI 1min	96.5±11.217	76.33±8.899	88.27±9.681	0
DBP AI 5min	86.37±6.066	74.93±8.606	81.33±15.94	0.054
DBP AP 1min	98.32±11.211	77.37±8.406	92.97±10.656	0
DBP AP 5min	94.73±11.216	79.03±7.636	94.37±10.761	0
DBP AP 15min	99.67±8.393	79.6±7.309	95.27±10.471	0
DBP AP 30min	94.18±11.118	77.4±8.904	91.03±12.016	0
DBP AP 45min	92.58±9.61	76.77±7.994	87.87±11.655	0
DBP PR	83.21±8.048	73.97±8.791	74.57±29.726	0.083
DBP AE	74.79±40.052	61.93±8.432	67.7±35.967	0
MAP preop	93.27±6.887	90.7±8.412	93.03±6.843	0
MAP AI 1min	113.97±12.253	89.83±8.595	100.47±9.343	0
MAP AI 5min	93.84±42.138	88.27±8.094	91.5±12.292	0.112
MAP AP 1min	114.68±11.407	92.03±7.573	104.4±10.536	0

MAP AP 5min	110.47±12.096	93.8±6.682	106.13±9.864	0
MAP AP 15min	111.08±48.14	94.33±6.222	106.47±9.698	0.002
MAP AP 30min	105.5±11.825	93±7.529	105.4±10.978	0
MAP AP 45min	103.87±10.246	92.1±6.984	101.73±11.064	0
MAP PR	61.92±40.494	48.93±24.125	51.87±42.282	0.094
MAP AE	95.42±18.797	82.27±20.671	87.93±39.471	0

Inference

a) Since the p value of heart rate pre op, AI 1 min, AP 1 min, AP 5 min, AP 15 min, AP 30 min, AP 45 min, and AE are lesser than 0.05, there is significant relationship between the group 1,2 and 3 and the variable. Based on the mean table, it can be concluded that the heart rate of group one is greater than group 3 and group 3 is greater than group 2.

b) Since the p value of heart rate AI 5 min and Heart rate PR greater than 0.05, there is no significant relationship between the group 1,2 and 3 and the variables.

c) Since the p value of Systolic blood pressure pre op, SBP AI 1 min, SBP AP 1 min, SBP AP 5 min, SBP AP 15 min, SBP AP 30 min, SBP AP 45 min and SBP AE are lesser than 0.05, there is significant relationship between the group 1,2 and 3 and the variable. Based on the mean table, it can be concluded that the Systolic blood pressure of group 1 is greater than group 3 and group 3 is greater than group 2.

d) Since the p value of systolic blood pressure AI 5 min and SBP PR greater than 0.05, there is no significant relationship between the group 1,2 and 3 and the variables

e) Since the p value of Diastolic blood pressure pre op, DBP AI 1 min, DBP AP 1 min, DBP AP 5 min, DBP AP 15 min, DBP AP 30 min, DBP AP 45 min and DBP AE are lesser than 0.05, there is significant relationship between the group 1,2 and 3 and the variable. Based on the mean table, it can be concluded that the Diastolic blood pressure of group one is greater than group 3 and group 3 is greater than group 2.

f) Since the p value of diastolic blood pressure AI 5 min and DBP PR greater than 0.05, there is no significant relationship between the group 1,2 and 3 and the variables

g) Since the p value of MAP pre op, MAP AI 1 min, MAP AP 1 min, MAP AP 5 min, MAP AP 15 min, MAP AP 30 min, MAP AP 45 min and MAP AE are lesser than 0.05, there is significant relationship between the group 1,2 and 3 and the variable. Based on the mean table, it can be concluded that the MAP of group 1 is greater than group 3 and group 3 is greater than group 2.

h) Since the p value of MAP AI 5 min and MAP PR greater than 0.05, there is no significant relationship between the group 1,2 and 3 and the variables

Figure 9. Comparing Heart rate in group1,2 & 3.

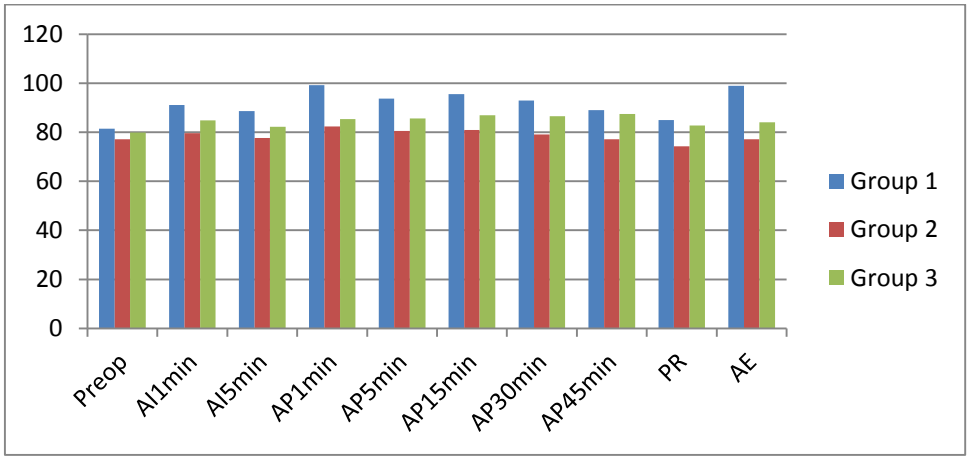


Figure 10. Comparing SBP in group1,2 & 3.

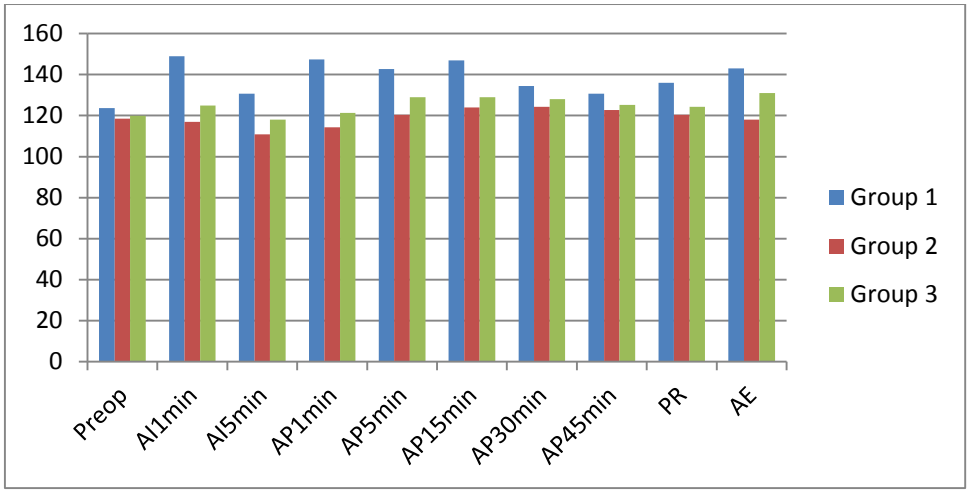


Figure 11. Comparing DBP in group1,2 & 3.

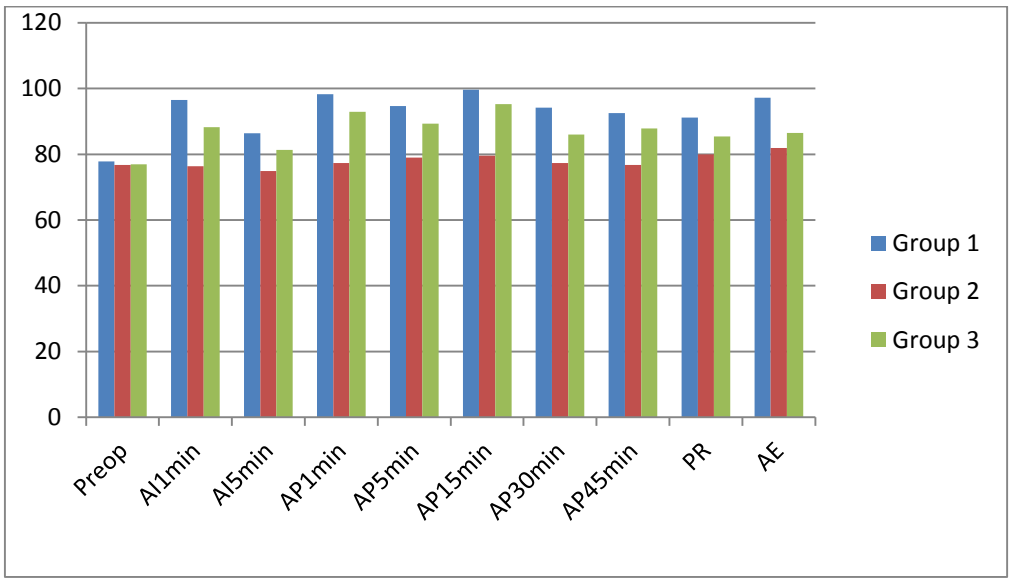


Figure 12. Comparing MAP in group1,2 & 3.

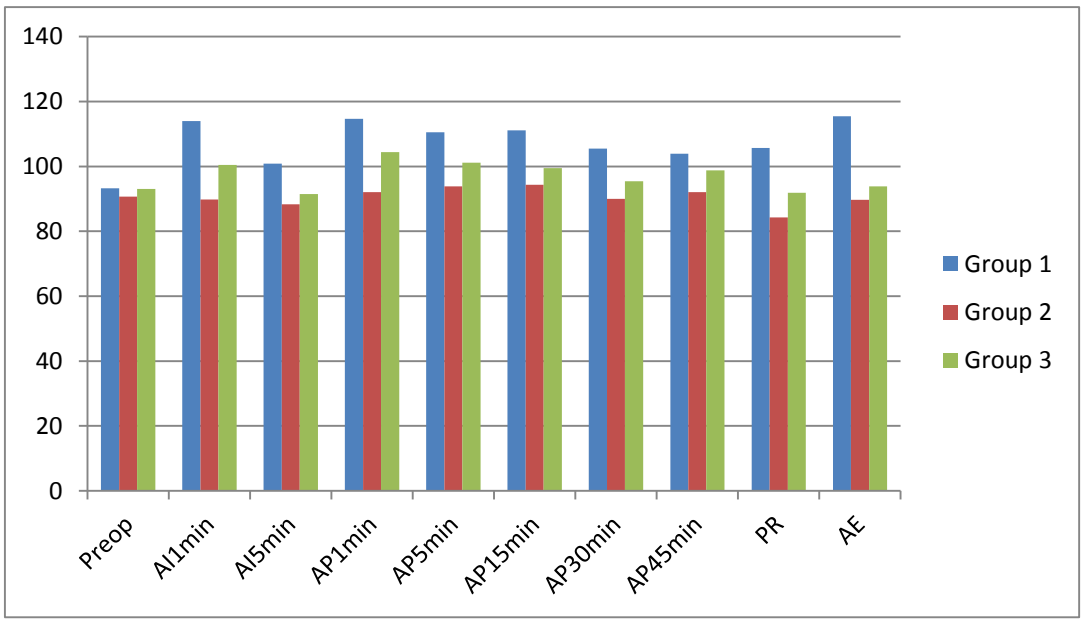


Figure 13. Comparing HR in group1,2 & 3

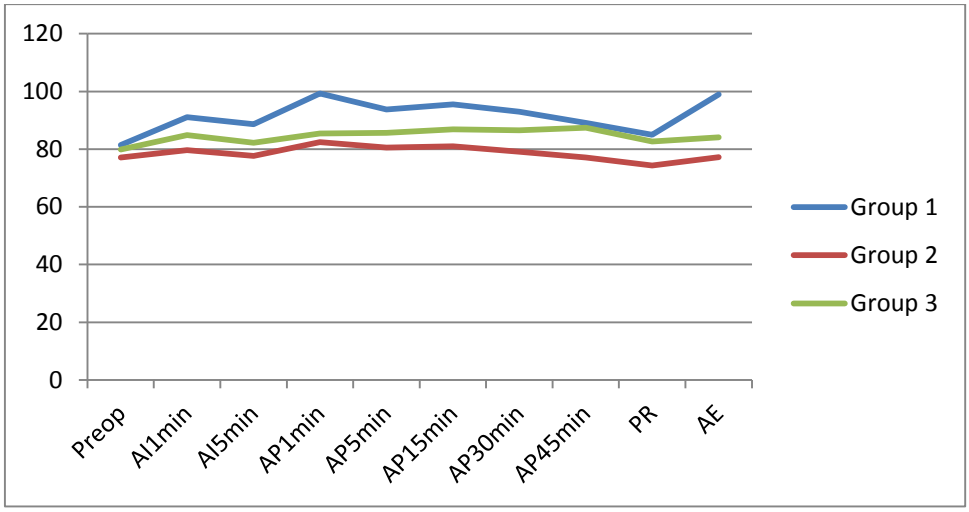


Figure 14. Comparing SBP in group1,2 & 3

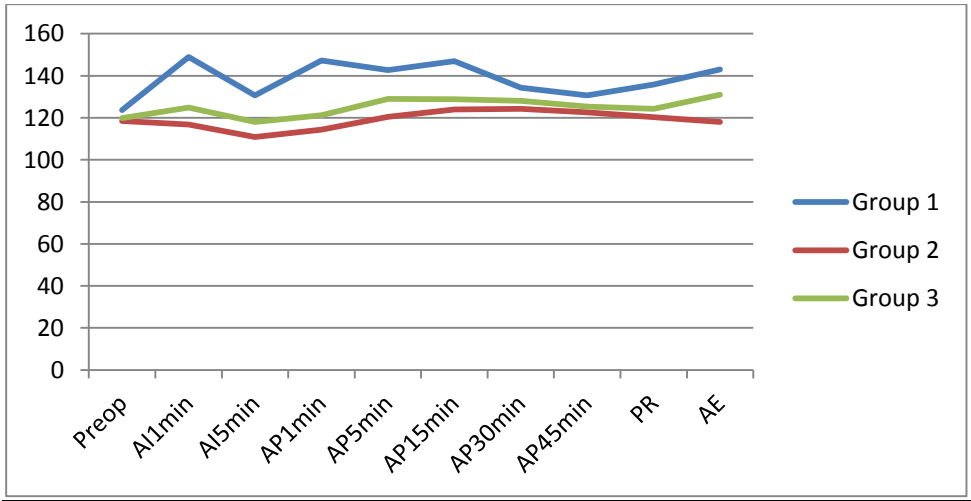


Figure 15. Comparing DBP in group1,2 & 3

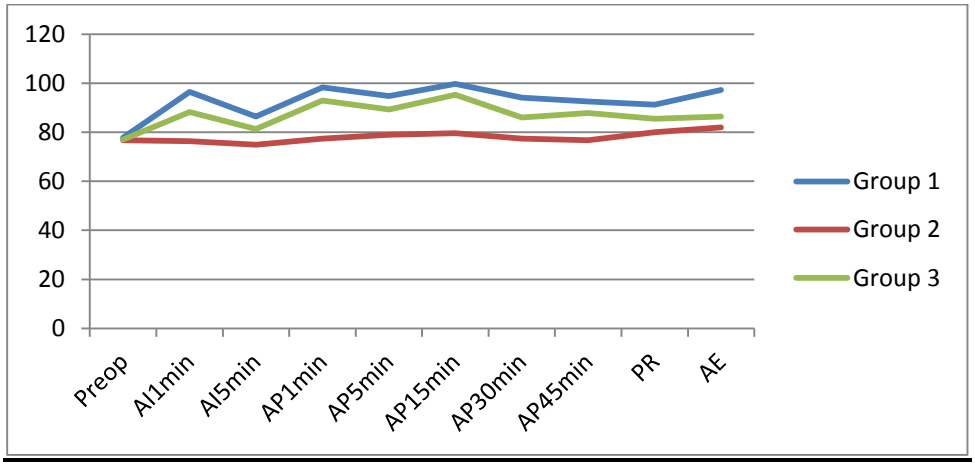


Figure 16. Comparing MAP in group1,2 & 3

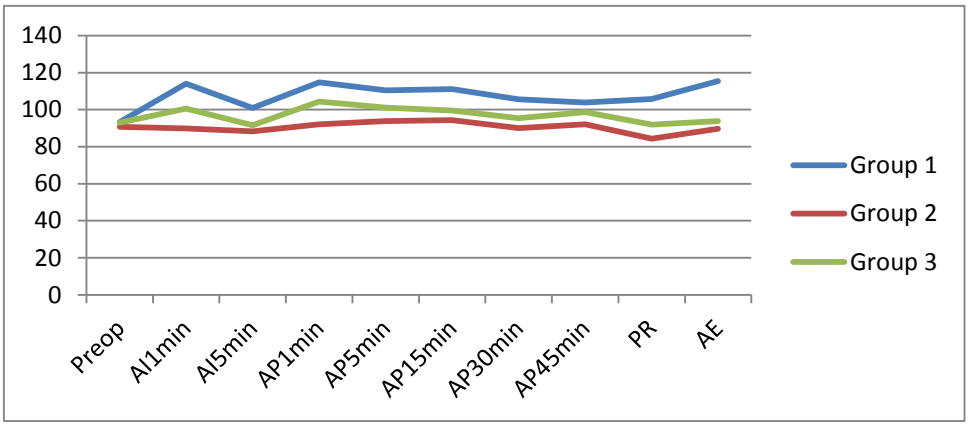


Table 4.Comparison of HR, SBP, DBP and MAP with group 1 and 2

GROUP	1 **(Mean±SD)**	2 **(Mean±SD)**	p value
HR preop	81.39±5.091	77.13±5.734	0.032
HR AI 1min	91.08±8.423	79.63±5.786	0
HR AI 5min	88.6±4.868	77.67±6.11	0.07
HR AP 1min	99.26±9.83	82.4±6.134	0
HR AP 5min	93.79±11.989	80.53±6.852	0
HR AP 15min	95.57±9.676	80.93±6.512	0
HR AP 30min	92.95±7.763	78.13±6.986	0
HR AP 45min	89.05±5.337	77.1±7.029	0
HR PR	84.95±4.893	74.3±6.587	0.434
HR AE	77.39±36.403	79.33±4.656	0
SBP preop	123.68±9.779	118.47±9.475	0.03
SBP AI 1min	148.97±16.747	116.87±11.443	0
SBP AI 5min	130.73±9.27	114.83±10.596	0.99
SBP AP 1min	147.34±13.921	124.3±9.444	0
SBP AP 5min	142.74±16.003	123.4±8.439	0

SBP AP 15min	146.97±10.545	123.9±7.522	0
SBP AP 30min	134.37±16.534	124.2±8.556	0.003
SBP AP 45min	130.61±13.962	122.67±8.727	0.008
SBP PR	11.92±1.075	10.1±15.302	0.384
SBP AE	14.21±1.473	11.37±0.964	0
DBP preop	77.82±6.939	76.8±9.155	0.004
DBP AI 1min	96.5±11.217	76.33±8.899	0
DBP AI 5min	86.37±6.066	74.93±8.606	0.51
DBP AP 1min	98.32±11.211	77.37±8.406	0
DBP AP 5min	94.73±11.216	79.03±7.636	0
DBP AP 15min	99.67±8.393	79.6±7.309	0
DBP AP 30min	94.18±11.118	77.4±8.904	0
DBP AP 45min	92.58±9.61	76.77±7.994	0
DBP PR	83.21±8.048	73.97±8.791	0.09
DBP AE	74.79±40.052	61.93±8.432	0.022
MAP preop	93.27±6.887	90.7±8.412	0.004
MAP AI 1min	113.97±12.253	89.83±8.595	0
MAP AI 5min	93.84±42.138	88.27±8.094	0.285
MAP AP 1min	114.68±11.407	92.03±7.573	0

MAP AP 5min	110.47±12.096	93.8±6.682	0
MAP AP 15min	111.08±48.14	94.33±6.222	0.015
MAP AP 30min	105.5±11.825	93±7.529	0
MAP AP 45min	103.87±10.246	92.1±6.984	0
MAP PR	61.92±40.494	48.93±24.125	0.066
MAP AE	95.42±18.797	82.27±20.671	0

Inference

a) Since the p value of heart rate pre op, AL 1 min, AP 1 min, AP 5 min, AP 15 min, AP 30 min, AP 45 min and HR AE are lesser than 0.05, there is significant relationship between the group 1and 2 and the variable. Based on the mean table, it can be concluded that the heart rate of group one is greater than group 2.

b) Since the p value of heart rate AL 5 min and Heart rate PR greater than 0.05, there is no significant relationship between the group 1 and 2 and the variables.

c) Since the p value of SBP pre op, AL 1 min, AP 1 min, AP 5 min, AP 15 min, AP 30 min, AP 45 min and SBP AE are lesser than 0.05, there is significant relationship between the group 1 and 2 and the variable. Based on the mean table, it can be concluded that the heart rate of group one is greater than group 2.

d) Since the p value of SBP AL 5 min and SBP PR greater than 0.05, there is no significant relationship between the group 1 and 2 and the variables.

e) Since the p value of DBP pre op, AL 1 min, AP 1 min, AP 5 min, AP 15 min, AP 30 min, AP 45 min and DBP AE are lesser than 0.05, there is significant relationship between the group 1 and 2 and the variable. Based on the mean table, it can be concluded that the heart rate of group one is greater than group 2.

f) Since the p value of DBP AL 5 min and DBP PR greater than 0.05, there is no significant relationship between the group 1 and 2 and the variables.

g) Since the p value of MAP pre op, AL 1 min, AP 1 min, AP 5 min, AP 15 min, AP 30 min, AP 45 min and MAP AE are lesser than 0.05, there is significant relationship between the group 1 and 2 and the variable. Based on the mean table, it can be concluded that the heart rate of group one is greater than group 2..

h) Since the p value of MAP AL 5 min and MAP PR greater than 0.05, there is no significant relationship between the group 1 and 2, and the variables.

Table 5.Comparison of HR, SBP, DBP, MAP with group 1 and 3

GROUP	1 **(Mean±SD)**	3 **(Mean±SD)**	P value
HR preop	81.39±5.091	79.9±5.845	0.004
HR AI 1min	91.08±8.423	84.83±6.502	0.001
HR AI 5min	88.6±4.868	82.23±5.557	0.07
HR AP 1min	99.26±9.83	91.37±7.937	0.001
HR AP 5min	93.79±11.989	92.37±7.591	0.019
HR AP 15min	95.57±9.676	93.9±7.053	0.009
HR AP 30min	92.95±7.763	86.5±7.243	0.016
HR AP 45min	89.05±5.337	87.4±7.025	0.002
HR PR	84.95±4.893	83.8±3.978	0.442
HR AE	77.39±36.403	74.43±30.978	0.017
SBP preop	123.68±9.779	119.83±9.158	0.002
SBP AI 1min	148.97±16.747	124.87±12.719	0
SBP AI 5min	130.73±9.27	118.03±10.833	0.27
SBP AP 1min	147.34±13.921	121.3±14.089	0
SBP AP 5min	142.74±16.003	128.93±14.225	0
SBP AP 15min	146.97±10.545	128.9±13.33	0
SBP AP 30min	134.37±16.534	128.07±14.701	0.006
SBP AP 45min	130.61±13.962	125.27±14.946	0.034
SBP PR	111.92±1.075	111.8±1.375	0.685

SBP AE	116.21±1.473	115.1±1.296	0
DBP preop	77.82±6.939	76.97±6.636	0
DBP AI 1min	96.5±11.217	88.27±9.681	0.002
DBP AI 5min	86.37±6.066	81.33±15.94	0.111
DBP AP 1min	98.32±11.211	92.97±10.656	0.05
DBP AP 5min	94.73±11.216	94.37±10.761	0.003
DBP AP 15min	99.67±8.393	95.27±10.471	0.008
DBP AP 30min	94.18±11.118	91.03±12.016	0.005
DBP AP 45min	92.58±9.61	87.87±11.655	0.044
DBP PR	83.21±8.048	74.57±29.726	0.06
DBP AE	74.79±40.052	67.7±35.967	0.05
MAP preop	93.27±6.887	93.03±6.843	0.001
MAP AI 1min	113.97±12.253	100.47±9.343	0
MAP AI 5min	93.84±42.138	91.5±12.292	0.091
MAP AP 1min	114.68±11.407	104.4±10.536	0
MAP AP 5min	110.47±12.096	106.13±9.864	0.006
MAP AP 15min	111.08±48.14	106.47±9.698	0
MAP AP 30min	105.5±11.825	105.4±10.978	0.002
MAP AP 45min	103.87±10.246	101.73±11.064	0.004
MAP PR	61.92±40.494	51.87±42.282	0.322
MAP AE	95.42±18.797	87.93±39.471	0.003

Inference

a) Since the p value of heart rate pre op, AL 1 min, AP 1 min, AP 5 min, AP 15 min, AP 30 min, AP 45 min and HR AE are lesser than 0.05, there is significant relationship between the group 1and 2 and the variable. Based on the mean table, it can be concluded that the heart rate of group one is greater than group 3.

b) Since the p value of heart rate AL 5 min and Heart rate PR greater than 0.05, there is no significant relationship between the group 1 and 3 and the variables.

c) Since the p value of SBP pre op, AL 1 min, AP 1 min, AP 5 min, AP 15 min, AP 30 min, AP 45 min and SBP AE are lesser than 0.05, there is significant relationship between the group 1 and 3 and the variable. Based on the mean table, it can be concluded that the heart rate of group one is greater than group 3.

d) Since the p value of SBP AI 5 min and SBP PR greater than 0.05, there is no significant relationship between the group 1 and 3 and the variables.

e) Since the p value of DBP pre op, AI 1 min, AP 1 min, AP 5 min, AP 15 min, AP 30 min, AP 45 min and DBP AE are lesser than 0.05, there is significant relationship between the group 1 and 3 and the variable. Based on the mean table, it can be concluded that the heart rate of group one is greater than group 3.

f) Since the p value of DBP AL 5 min and DBP PR greater than 0.05, there is no significant relationship between the group 1 and 3 and the variables.

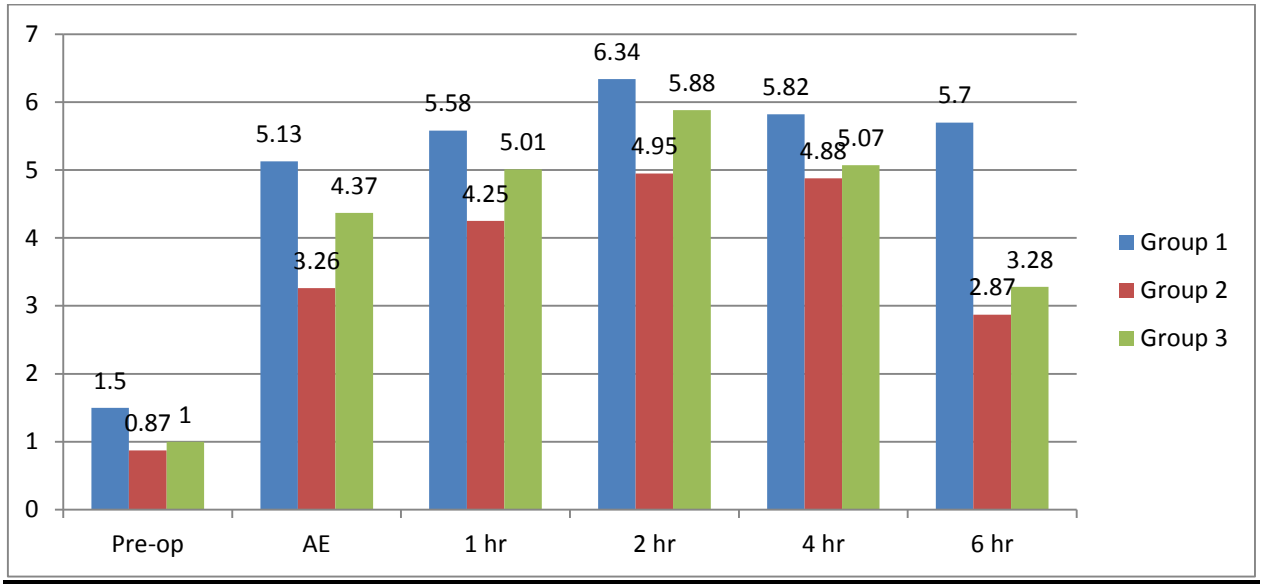
g) Since the p value of MAP pre op, AL 1 min, AP 1 min, AP 5 min, AP 15 min, AP 30 min, AP 45 min and MAP AE are lesser than 0.05, there is significant relationship between the group 1 and 3 and the variable. Based on the mean table, it can be concluded that the heart rate of group one is greater than group 3.

h) Since the p value of MAP AI 5 min and MAP PR greater than 0.05, there is no significant relationship between the group 1 and 3, and the variables.

Table 6.Vas score comparison

VAS	Group 1**(Mean±SD)**	Group 2 **(Mean±SD)**	Group 3 **(Mean±SD)**	P value
Pre-op	1.5±0.507	0.87±0.575	1.0±0.458	0.00
AE	5.13±0.704	3.26±0.826	4.37±0.527	0.05
1 hr	5.58±0.599	4.25±0.528	5.01±0.957	0.002
2 hr	6.34±0.627	4.95±0.113	5.88±0.492	0.015
4 hr	5.82±0.563	4.88±0.368	5.07±0.492	0.03
6 hr	5.79±0.528	2.87±0.673	3.28±0.992	0.00

Figure 17. Comparing VAS Score in group1,2 & 3



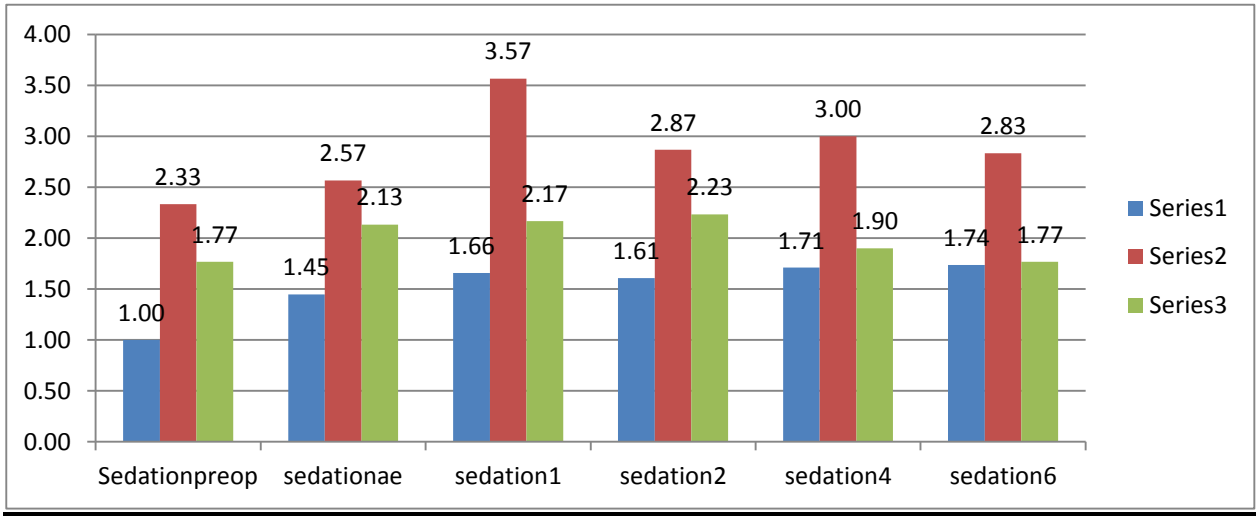
Inference

There is a significant relationship between the VAS score of group 1, 2 and 3. Based on the mean, the VAS score of group 2 is less than group 3 which is less than group 1.

Table 7.Sedation score

	Group 1 **(Mean±SD)**	Group 2 **(Mean±SD)**	Group 3 **(Mean±SD)**	P value
Pre op	1±0.21	2.33±0.479	1.77±0.626	0.000
AE	1.45±0.686	2.57±0.504	2.13±0.571	0.028
1 hr	1.66±0.669	3.57±0.504	2.17±0.592	0.001
2 hr	1.61±0.495	2.87±0.434	2.23±0.679	0.006
4 hr	1.71±0.46	3±0.371	1.9±0.803	0.000
6 hr	1.74±0.446	2.83±0.531	1.77±0.898	0.002

Figure 18. Comparing Sedation score in group1,2 & 3



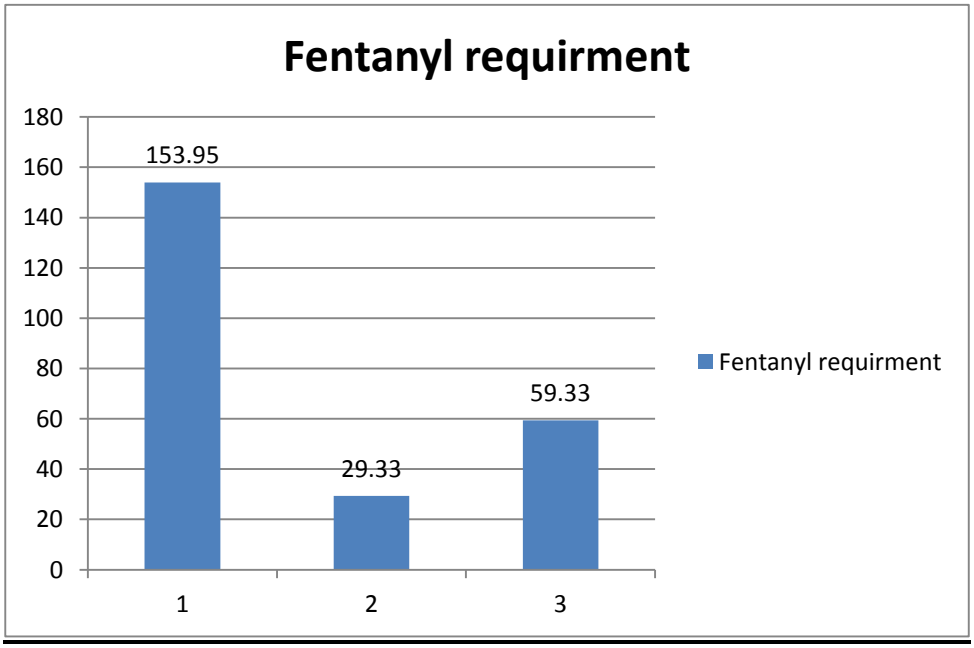
Inference

There is a significant association between the sedation score of group 1, 2 and 3. The sedation score of group 2 is greater than group 3 which is in turn greater than group 1.

Table 8.Fentanyl requirement

Group	1 **(Mean±SD)**	2 **(Mean±SD)**	3 **(Mean±SD)**	p-value
Mean	153.95±27.365	29.33±15.071	59.33±21.645	0.004

Figure 19. Comparing Fentanyl requirement in group1,2 & 3



Inference

There is a significant difference between the Fentanyl requirement in group 1, 2 and 3. Group 1 requires more than group 3 and group 3 requires more than group 2.

Table 9.Side effects

Group	Nausea	Vomitting	Drowsiness
1	2 (2.1%)	3 (3.1%)	3 (3.1%)
2	1 (1.1%)	2 (2.1%)	13 (13.3%)
3	2 (2.1%)	3 (3.1%)	5 (5.1%)

Inference

Drowsiness is more common in group 2 than other groups. Other side effects were having insignificant difference among the groups.

DISCUSSION

During laparoscopy pneumoperitoneum produces significant haemodynamic changes, which are well tolerated in normal healthy patients but in patients with compromised cardiorespiratory function are detrimental. Various pharmacological drugs have been used to counteract these hemodynamic effects of pneumoperitoneum. This study was carried out in 90 adult patients, to evaluate the effect of oral clonidine 200 µg and pregabalin 150 mg in attenuating haemodynamic stress response associated with pneumoperitoneum.

Clonidine, is a selective α2 adrenergic agonist and an imidazoline derivative . It is an antihypertensive drug. It produces a fall in the heart rate and blood pressure associated with decreased SVR and cardiac output. Clonidine inhibits the vasopressin and catecholamine release and there by modulates the haemodynamic changes produced by pneumoperitoneum.

Joris et al[17] used very high dose of clonidine (8 µg/kg) for reducing catecholamine and vasopressin levels following pneumoperitoneum. Aho et al used 3 µg/kg and 4.5 µg/kg clonidine for suppression of haemodynamic response to pneumoperitoneum. Malek et al[6] used 150 µg of clonidine as i.v. infusion and intramuscularly while Sung et al[11] and Yu et al [7]used 150 µg of oral clonidine as premedication for maintenance of haemodynamic stability during pneumoperitoneum.

In my study 200µg of oral Clonidine was used given 60 minutes before induction, there was no significant rise in the heart rate throughout the intra operative period.

Kumkum gupta et al[4] in 2011 analysed oral premedication with pregabalin (150mg) Group II or clonidine (200microgram) Group III given 75 to 90 mins before surgery as oral premedication.

In my study I used the same dosage of pregabalin and clonidine given orally 60 mins before surgery.

In my study the placebo group had hemodynamic instability in the form of rise in heart rate, systolic BP, diastolic BP and mean arterial pressure, but in clonidine and pregabalin group there is no rise in BP throughout the surgery maintaining the haemodynamic stability. The difference is statistically significant. Clonidine has a better stability than the pregabalin group.

Clonidine interacts with the endogenous opiates beta-endorphins. The plasma level of beta-endorphins increases significantly after laproscopy. The blunting effect of clonidine on hemodynamics and plasma beta-endorphins may reflect a deeper level of anaesthesia in those receiving Clonidine.

Marimony et al[8] (2007) found “a decreased incidence of nausea and vomiting in patients receiving Clonidine. Clonidine increases gastrointestinal motility by decreasing sympathetic outflow and increasing parasympathetic

outflow from the central nervous system". Though many workers have reported the antiemetic property of clonidine, the mechanism by which it acts needs further investigation.

There was a reduction in the PONV in patients receiving Clonidine , as compared to control and pregabalin. But this reduction is not statistically significant.

Sung et al[11] (2000) and Yu et al[7] (2003) found that preoperative clonidine admistration reduced the post operative analgesic requirement. In my study also there was a significant reduction in the post operative analgesic requirement in patients receiving clonidine. Pregabalin group also had reduced post operative analgesic requirement but the reduction in pregabalin group is less than the clonidine group.

In my study the post operative sedation score was observed for 6 hrs postoperatively and was found that clonidine group had a significantly high sedation score than other groups.

It was observed that post operative anti emetic requirement was insignificant in all the groups.

There is a significant difference between the Fentanyl requirement in group 1, 2 and 3. Group 1 requires more than group 3 and group 3 requires more than group 2.

Post operative analgesic requirement was also observed to be significantly lower in Clonidine groupand pregabalin group as compared to the placebo group. It was found to be more decreased in clonidine group than with pregabalin group.

There is a significant association between the sedation score of group 1, 2 and 3. The sedation score of clonidine group is greater than pregabalin group which is in turn greater than placebo group .

No adverse effect was observed with the study group during the intra operative and post operative period.

SUMMARY

Haemodynamicchanges during laparoscopic surgery is attributed to the stress response to pneumoperitonium.

We studied ninety patients of both sexes coming toTirunelveli edical College hospital for elective laparoscopic surgeries. The patients were randomized in to three groups to receive placebo tablet in group I, 200 microgram of clonidine in Group II and 150 mg of pregabalin in group III about 60 mins before induction of anaesthesia.Patients were observed for intra operative heart rate, systolic BP, diastolic BP and mean BP. Hemodynamic instability was defined as heart rate and blood pressure fall or rise not more than 15% from base line.

Both Clonidine and pregabalin were effective in producing intra operative hemodynamic stability as compared to the control group by blunting the stress response to pneumoperitonium but the hemodynamic stability is better with clonidine group than pregabalin group, which itself is better than placebo group.

The pain scores was significantly reduced in clonidine and pregabalin groups when compared to the placebo group but the reduction in scores in the pregabalin group is significantly less than thatof the clonidine group.

The sedation score is higher in clonidine group when compared to placebo and pregabalin.

Intraoperative fentanyl requirement is more with placebo group than pregabaline group , which itself higher than clonidine group.

Drowsiness is more with clonidine group than pregabalin and placebo.

Post operative nausea and vomiting incidence was similar in all groups.

CONCLUSION

This study showed that an oralpremedication dose of clonidine of 200 µgor oral dose of pregabalin 150 mg attenuated the hemodynamic stress response produced by laryngoscopy and pneumoperitonium in patients undergoing laparoscopic surgeries. It showed that oral clonidine 200 µgproduced better hemodynamic stability than oralpregabalin 150mg. Intra operative opioid requirement and postoperative pain score was reduced in both clonidine and pregabalin than placebo group but better reduction with clonidine. The sedation score was high in clonidine when compared to pregabaline and placebo. Post op drowsiness was more with clonidine than pregabalin and placebo.

This study concluded that oral premedication with Clonidine200 µg and Pregabalin 150mg produces betterhemodynamic stability in laparoscopic surgeries but Clonidine produces better haemodynamic stability than Pregabalin.Both drugs has significantly reduces intraoperative and post operative analgesic requirements without significant post operative respiratory depression.

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PROFORMA

COMPARISON OF EFFECTS OF ORAL CLONIDINE AND PREGABALIN FOR HAEMODYNAMIC STABILITY DURING LAPAROSCOPIC SURGERIES- A PROSPECTIVE RANDOMIZED PLACEBO CONTROL STUDY

GROUP-

NAME AGE IP NO WT

PRE MED - Study drug / Placebo

PRE INDUCTION - Glycopyrrolate 0.2mg & Midazolam- 0.03 mg/kg

INDUCTION- Propofol 2mg/kg Fentanyl 2 mics/kg Vecuronium 0.1mg/kg

MAINTANANCE- Oxygen:NitrousOxide 2:3 ,Vecuronium, Fentanyl -20mics half hrly (if additional analgesic required suppl with 10 mics)

MONITORING PARAMETERS

	PR	SBP	DBP	MAP
Base line				
Pre-op				
AI 1 Min				
AI 5 min				
AP 1 min				
AP 5 min				
AP 15 min				
AP 30 min				
AP 45 min				
PR				

AE				

REVERSAL- Neostigmine- 0.5mg/kg

Glycopyrrolate- 0.01mg/kg

Pain score: Preop, AE, 1 Hr, 2 Hr, 4 Hr and 6 Hr.

Sedation score: Preop, AE, 1 Hr, 2 Hr, 4Hr and 6 Hr.

TOTAL FENTANYL REQUIREMENT -

COMPLICATIONS –

Nausea: present / absent

Vomiting: present / absent

Drowsiness: present / absent

ஆராய்ச்சி ஒப்புதல் படிவம்

லாப்பிராஸ்கோபி அறுவை சிகிச்சையின் போது இதயத்துடிப்பு மற்றும் இரத்த அழுத்தத்தில் ஏற்படும் மாறுதல்களை Clonidine மற்றும் Pregabalin என்ற இருவேறு மாத்திரைகளை கொண்டு ஒப்பீடும் ஆய்வு.

பெயர் :

வயது :

இனம் :

உள்நோயாளி எண்:

வார்டு :

நோய் :

அறுவை சிகிச்சை :

விளக்கம்:

லாப்பிராஸ்கோபி அறுவை சிகிச்சையின் போது இதயத் துடிப்பு மற்றும் இரத்த அழுத்தத்தில் ஏற்படும் மாறுதல்களை Clonidine மற்றும் Pregabalin என்ற இருவேறு மாத்திரைகளை மயக்க மருந்து செலுத்துவதற்கு சரியாக 1 மணி நேரத்திற்கு முன்பு வாய் வழியாக உட்கொள்வதால் ஏற்படும் பலன்கள், விளைவுகள், பக்க விளைவுகள் பற்றி எனக்கு நன்கு புரிகின்ற தமிழ் மொழியில் தெளிவாக விளக்கி கூறப்பட்டது. என்னுடைய அடையாளம் எந்த வகையிலும் இந்த ஆராய்ச்சி மூலம் வெளியே தெரியாது என்பதை அறிவேன். இந்த ஆராய்ச்சியில் இருந்து எந்த நேரமும் விலகலாம் என்பதையும் அதனால் எந்த பாதிப்பும் ஏற்படாது என்பதையும் அறிவேன்.

நான் யாருடைய நிர்பந்தமின்றி என் சொந்த விருப்பத்தின் பேரில் சுயநினைவுடன் இந்த ஆராய்ச்சியில் பங்கு கொள்ள சம்மதிக்கிறேன்.

இடம்:
நாள்: கையொப்பம்

S.NO	AGE	SEX	GROUP	ASA	BASELINE PARAMETERS				DURATION	HEART RATE									
					HR	SBP	DBP	MAP		PREOP	AI		AP					PR	AE
											1 MIN	5 MIN	1 MIN	5 MIN	15 MIN	30 MIN	45 MIN		
1	35	F	1	1	72	116	68	84	60	83	90	88	95	90	92	80	85	78	95
2	37	F	1	2	72	140	86	104	60	80	120	80	121	95	95	80	79	78	98
3	48	F	1	2	80	136	88	104	45	86	92	90	102	98	98	84	82	84	102
4	43	F	1	1	78	134	81	98	45	92	96	90	98	92	92	80	82	80	96
5	44	M	1	2	74	110	70	83	50	79	84	80	107	76	77	76	78	76	92
6	49	M	1	1	86	126	80	95	50	89	92	90	92	80	81	90	92	90	108
7	39	F	1	2	71	120	78	91	50	74	98	95	111	97	98	100	91	86	99
8	46	F	1	1	70	124	82	95	60	74	81	78	88	76	77	80	82	80	94
9	45	M	1	2	76	110	71	83	60	78	98	87	125	120	122	90	93	80	95
10	48	F	1	1	76	124	83	96	55	78	82	87	105	92	93	78	80	78	94
11	50	F	1	1	88	140	86	104	55	88	97	90	98	91	92	88	80	82	90
12	54	M	1	2	78	140	82	101	45	80	89	85	99	96	99	90	89	88	95
13	45	M	1	1	86	132	81	97	45	85	94	90	105	109	100	97	95	89	100
14	51	F	1	1	85	120	70	86	45	87	90	90	100	102	103	98	90	83	95
15	37	M	1	2	83	110	70	83	60	80	89	85	90	95	99	90	88	85	99
16	42	M	1	1	78	132	81	97	60	80	95	90	101	108	105	99	90	89	105
17	39	F	1	1	75	116	68	84	60	78	87	85	97	98	98	98	90	86	90
18	51	F	1	2	88	136	88	104	60	86	97	90	105	100	100	95	89	89	93
19	43	F	1	1	79	120	70	86	60	85	90	89	98	88	88	82	84	72	99
20	52	F	1	1	68	106	71	82	55	74	85	79	100	76	77	88	90	88	92
21	40	M	1	1	76	132	78	95	55	82	100	95	104	96	98	86	88	86	96
22	32	F	1	1	82	140	82	101	55	84	90	90	98	87	88	85	87	85	89
23	54	M	1	2	75	142	84	103	55	79	93	85	92	86	87	75	77	75	99
24	58	F	1	2	71	118	72	87	50	75	97	90	98	97	98	88	90	88	95
25	60	F	1	2	78	128	82	97	50	84	100	90	110	107	107	100	97	86	101
26	55	F	1	2	83	120	74	89	50	85	98	95	108	100	100	98	90	90	99
27	50	M	1	1	79	113	60	83	50	80	98	90	102	105	106	99	94	91	97
28	44	M	1	1	85	134	81	98	60	85	98	97	111	110	100	97	90	90	97
29	42	F	1	1	84	116	68	84	60	86	94	93	99	95	97	95	97	89	94
30	40	F	1	1	87	134	81	98	60	88	96	95	98	106	100	97	94	90	105
31	46	F	2	1	88	120	74	89	45	71	74	72	77	71	77	68	66	62	78
32	54	M	2	2	82	132	81	97	45	79	80	80	83	87	89	80	82	80	81
33	56	F	2	2	79	113	69	83	45	77	81	79	80	85	85	70	72	70	84
34	60	F	2	1	77	120	70	86	50	71	74	72	77	71	72	74	70	72	74
35	58	F	2	2	80	112	70	83	50	73	75	70	76	73	73	74	72	70	72
36	36	M	2	1	84	130	84	99	50	72	75	75	74	70	72	68	66	64	70
37	37	M	2	2	83	142	91	107	60	80	82	82	89	80	80	80	82	80	81
38	32	M	2	1	79	123	79	93	60	78	80	80	82	74	74	72	70	72	80
39	56	F	2	1	78	130	80	96	55	72	77	75	78	70	70	70	71	70	75
40	44	F	2	2	79	122	80	93	60	74	80	76	81	76	76	73	72	70	81
41	45	F	2	1	84	110	64	79	45	89	92	90	95	87	87	83	80	81	88
42	48	F	2	2	68	122	71	87	55	74	76	76	78	72	70	70	71	70	75
43	42	F	2	2	86	110	59	75	50	80	84	80	88	89	82	82	80	82	82
44	40	M	2	1	76	110	60	76	55	82	82	80	84	81	82	82	80	72	80
45	39	F	2	1	86	120	80	93	55	76	76	74	77	78	78	75	77	70	76
46	45	M	2	2	85	102	72	81	45	81	82	80	86	88	88	74	73	74	81
47	56	F	2	2	86	132	78	95	45	74	79	70	78	78	78	77	75	71	75
48	33	F	2	1	79	114	66	81	60	78	78	78	80	81	82	82	80	80	80
49	36	M	2	1	78	128	68	87	60	71	74	70	74	76	77	77	70	66	70
50	39	M	2	1	86	120	68	85	60	69	70	70	76	78	78	78	80	70	77
51	40	F	2	2	85	128	86	99	60	71	74	72	79	79	80	82	80	74	80
52	49	F	2	2	88	120	93	101	60	79	82	78	95	88	88	66	64	65	78
53	38	F	2	1	80	112	82	91	60	88	89	89	90	89	90	89	86	75	80
54	32	F	2	2	90	112	82	91	60	78	84	80	85	82	83	80	81	78	80
55	42	M	2	1	79	122	66	84	55	80	88	83	86	88	88	89	85	80	84
56	33	M	2	1	84	136	78	97	55	89	89	89	91	93	92	90	85	87	87
57	45	M	2	2	89	140	77	98	55	84	86	86	90	90	90	89	90	82	84
58	38	M	2	1	78	117	83	94	55	74	72	70	78	78	80	80	81	74	79

S.NO	AGE	SEX	GROUP	ASA	BASELINE PARAMETERS				DURATION	HEART RATE									
					HR	SBP	DBP	MAP		PREOP	AI		AP					PR	AE
											1 MIN	5 MIN	1 MIN	5 MIN	15 MIN	30 MIN	45 MIN		
59	60	F	2	2	84	110	76	87	45	82	84	84	88	87	89	90	90	88	88
60	44	F	2	1	86	129	91	102	45	68	70	70	77	77	78	80	82	80	80
61	52	M	3	1	78	124	80	94	60	78	80	80	88	88	89	86	80	78	88
62	49	M	3	2	76	119	77	91	55	75	81	80	101	100	99	95	85	80	90
63	58	M	3	1	88	114	75	88	55	86	90	85	92	92	94	89	90	82	92
64	50	F	3	2	86	123	86	98	45	92	94	94	98	98	96	90	94	89	97
65	52	F	3	1	84	116	74	88	45	86	89	85	98	92	93	90	89	88	90
66	40	M	3	2	76	132	80	97	50	81	84	84	90	92	90	92	90	87	99
67	44	F	3	2	70	122	82	95	50	76	79	78	80	82	84	80	82	80	88
68	37	F	3	2	60	126	84	98	50	64	64	65	78	78	80	80	78	80	88
69	58	M	3	2	74	130	80	96	60	79	82	80	88	86	86	85	80	78	90
70	55	F	3	1	73	130	78	95	60	78	82	80	86	88	90	90	87	85	85
71	57	F	3	2	83	124	78	93	60	80	98	90	107	109	110	103	98	82	100
72	43	F	3	2	68	108	70	82	60	71	76	76	79	100	102	82	81	80	85
73	44	F	3	2	76	110	76	87	55	74	88	80	89	92	92	88	87	80	95
74	42	F	3	1	71	121	78	92	55	76	80	79	90	92	94	96	88	84	94
75	46	M	3	2	78	129	84	99	50	82	87	85	90	97	99	100	94	88	102
76	38	F	3	1	64	130	82	98	45	71	90	90	100	102	100	100	98	90	99
77	32	F	3	2	70	126	84	98	45	75	89	80	110	110	108	105	109	89	98
78	38	F	3	1	68	122	81	94	45	79	82	82	95	90	92	94	88	85	91
79	36	M	3	1	71	116	68	84	60	78	78	75	80	82	84	82	85	87	95
80	58	F	3	1	80	112	71	84	60	88	82	80	90	93	96	93	90	88	103
81	55	M	3	2	86	124	80	94	55	80	93	90	100	102	100	102	98	90	98
82	57	M	3	1	90	130	80	96	55	88	88	85	90	92	94	97	90	88	89
83	49	M	3	1	86	110	76	87	60	86	87	85	90	90	92	93	92	87	89
84	43	F	3	1	86	116	68	84	60	84	90	90	100	102	104	104	99	90	101
85	38	F	3	1	80	110	70	83	50	82	83	80	88	89	90	90	85	86	88
86	36	F	3	2	87	136	88	104	50	80	85	85	90	95	95	95	90	84	90
87	41	M	3	2	88	120	78	91	45	79	80	80	81	89	87	89	82	82	84
88	35	F	3	1	79	110	71	83	45	81	90	82	96	102	100	105	99	91	107
89	32	F	3	1	85	126	80	95	50	83	85	82	88	89	90	89	90	81	83
90	52	M	3	2	88	134	81	98	60	85	89	80	89	88	87	91	84	85	88

S.NO	SYSTOLIC BLOOD PRESSURE										DIASTOLIC BLOOD PRESSURE									
	PREOP	AI		AP					PR	AE	PREOP	AI		AP					PR	AE
		1 MIN	5 MIN	1 MIN	5 MIN	15 MIN	30 MIN	45 MIN				1 MIN	5 MIN	1 MIN	5 MIN	15 MIN	30 MIN	45 MIN		
1	116	142	130	140	145	140	120	118	120	139	76	101	80	112	100	112	90	88	77	99
2	140	134	128	142	148	146	142	140	128	133	80	92	86	99	99	100	87	89	87	74
3	136	162	140	150	160	156	138	122	124	148	86	120	90	122	120	122	110	100	86	108
4	134	154	130	149	145	144	127	130	117	160	80	90	88	102	96	98	90	88	80	100
5	110	133	128	144	141	142	138	130	114	142	78	103	88	108	102	100	98	96	90	102
6	126	162	148	166	158	158	150	143	130	158	88	100	90	110	108	110	108	100	90	106
7	120	128	124	138	132	132	128	128	116	130	71	88	80	92	90	92	90	92	90	92
8	124	142	130	148	140	140	142	138	130	139	82	98	94	100	100	100	99	92	92	89
9	110	128	122	144	150	152	152	140	130	136	62	86	76	90	90	92	88	88	80	96
10	124	144	136	148	162	164	112	114	112	139	70	80	80	90	86	88	88	82	86	90
11	126	136	124	138	130	130	134	128	124	130	86	90	88	94	96	98	94	90	92	94
12	110	124	118	132	134	136	140	130	128	138	76	86	80	88	88	90	84	84	80	88
13	124	138	120	146	140	141	142	132	118	128	88	94	92	96	90	92	92	88	82	90
14	120	160	130	170	160	162	162	150	130	142	80	100	92	108	110	108	102	94	88	94
15	118	128	122	138	142	144	146	140	130	138	70	83	80	94	91	92	90	89	87	92
16	122	138	128	148	152	156	160	150	130	150	78	88	86	100	102	104	106	98	98	96
17	134	154	130	149	145	140	127	130	114	142	84	99	90	102	100	102	99	90	88	101
18	120	170	130	160	166	160	150	152	132	142	80	110	88	108	112	114	110	99	90	100
19	120	171	136	178	166	154	136	114	112	162	70	108	99	110	104	106	96	64	62	100
20	106	109	110	124	118	128	102	104	102	105	69	80	76	90	81	84	79	67	77	89
21	132	163	142	154	141	138	136	128	126	157	74	102	90	111	99	100	87	90	78	90
22	140	165	142	166	160	158	152	148	138	152	71	92	90	110	104	102	100	96	88	102
23	142	169	150	158	131	130	127	129	127	171	84	106	98	112	105	106	101	96	80	105
24	118	167	126	164	154	150	124	128	116	159	71	111	91	114	100	100	99	92	88	99
25	128	151	132	154	150	146	142	132	130	148	82	96	90	101	93	92	107	103	97	93
26	128	150	132	154	148	146	142	138	128	150	86	90	82	98	98	99	92	90	88	101
27	130	144	132	152	148	150	150	148	132	142	70	88	82	96	96	98	90	89	82	95
28	114	128	120	140	142	144	146	130	130	140	70	80	80	92	90	92	89	88	79	89
29	122	160	148	166	170	166	152	146	132	146	88	90	85	108	105	104	100	94	90	98
30	132	146	134	162	160	156	160	160	140	148	78	89	80	99	92	93	90	90	80	94
31	110	108	106	112	116	118	115	116	110	110	77	78	77	82	82	84	72	72	70	72
32	129	110	110	126	126	128	130	132	118	120	82	82	80	86	84	86	86	82	78	80
33	117	120	118	122	120	124	126	124	116	118	71	72	70	77	77	79	70	72	68	70
34	118	116	110	117	118	120	122	120	118	120	72	75	71	72	74	77	74	70	66	68
35	114	112	110	114	120	122	114	116	112	110	74	72	72	75	74	75	75	74	70	71
36	120	120	120	126	130	132	132	132	120	122	87	84	80	82	84	88	84	81	80	82
37	139	146	140	142	140	137	140	142	138	130	92	90	90	92	94	92	94	92	88	90
38	130	132	130	132	134	132	130	128	122	120	81	80	80	82	84	86	83	82	78	78
39	128	132	126	136	130	132	136	136	134	132	82	83	80	82	82	80	78	80	76	79
40	124	122	122	124	130	132	134	126	122	122	84	82	82	80	84	82	82	84	80	81
41	100	99	98	110	110	112	112	112	108	100	61	62	60	64	71	72	68	69	60	62
42	119	126	120	116	126	122	120	122	118	100	72	75	70	74	74	74	70	72	68	69
43	114	117	120	130	132	132	132	130	128	130	61	60	60	62	66	66	60	62	58	60
44	108	100	100	107	108	110	112	110	100	104	62	60	61	64	67	68	67	62	60	61
45	110	110	108	120	126	124	122	124	118	110	77	75	77	79	78	78	77	77	75	75
46	104	102	102	110	110	110	109	106	103	100	75	78	78	76	80	80	82	80	77	78
47	130	130	130	135	132	132	135	131	126	122	80	80	77	82	83	83	85	79	80	80
48	115	113	110	112	122	120	116	114	110	112	68	66	65	70	72	72	70	71	69	70
49	131	130	130	132	134	130	130	132	126	120	70	70	71	70	72	72	66	68	64	64
50	125	128	120	127	128	130	132	128	120	120	72	70	68	68	69	70	68	72	68	68
51	126	120	120	124	126	128	130	124	120	124	88	85	83	87	87	86	86	86	88	86
52	122	120	117	122	128	126	127	124	119	120	94	90	91	92	93	93	92	90	90	90
53	116	110	110	117	118	120	120	116	112	116	84	84	80	84	82	82	82	84	80	80
54	110	110	108	108	110	112	114	112	102	108	84	85	80	80	84	84	80	82	78	78
55	112	104	100	110	116	118	118	118	110	110	64	64	64	68	70	71	64	66	62	65
56	119	120	120	128	128	128	130	126	122	120	76	77	76	70	78	78	79	72	74	75
57	122	109	110	118	120	120	120	119	109	106	83	80	80	85	86	88	86	82	80	80
58	103	100	100	110	112	114	114	110	95	100	67	65	65	68	70	72	70	71	69	68

S.NO	SYSTOLIC BLOOD PRESSURE										DIASTOLIC BLOOD PRESSURE									
	PREOP	AI		AP					PR	AE	PREOP	AI		AP					PR	AE
		1 MIN	5 MIN	1 MIN	5 MIN	15 MIN	30 MIN	45 MIN				1 MIN	5 MIN	1 MIN	5 MIN	15 MIN	30 MIN	45 MIN		
59	110	110	106	120	120	122	122	118	111	110	74	74	70	78	78	80	80	79	77	80
60	129	130	124	132	132	130	132	132	125	120	90	92	90	90	92	90	92	90	88	88
61	114	148	140	140	144	146	148	136	140	142	74	74	73	74	76	77	68	70	68	70
62	117	125	110	130	134	136	140	136	130	138	75	89	80	90	82	83	94	90	90	92
63	112	114	110	110	116	118	108	110	105	120	76	90	88	94	98	96	96	98	90	98
64	122	164	120	170	172	168	160	162	150	142	86	107	100	116	110	114	116	118	110	110
65	109	110	103	110	112	114	120	103	105	102	72	83	78	88	90	92	90	94	88	88
66	132	136	128	140	141	138	142	138	130	136	82	96	88	100	102	102	102	106	100	106
67	116	118	110	114	116	116	116	108	103	110	74	84	80	90	90	91	92	88	89	89
68	129	132	130	131	141	138	120	122	125	132	84	96	90	99	98	98	96	90	90	92
69	128	128	128	124	119	120	123	125	127	120	79	95	86	98	97	98	98	90	98	98
70	133	136	131	132	130	130	128	128	124	128	78	84	80	94	94	94	96	90	88	94
71	121	118	116	120	121	120	123	116	118	118	76	89	80	90	91	90	95	90	84	98
72	110	114	108	110	112	112	108	109	107	110	68	70	70	80	82	82	82	84	80	80
73	110	119	118	128	130	130	131	132	128	138	72	78	78	90	98	98	98	96	90	99
74	112	128	120	140	145	140	149	144	136	130	78	78	74	78	80	82	76	78	77	78
75	126	128	120	126	126	128	130	122	124	124	82	94	88	98	98	98	96	98	88	93
76	128	130	130	128	132	130	131	132	122	133	84	85	85	90	92	94	92	88	86	84
77	128	128	120	124	126	128	120	121	123	128	84	88	84	85	84	86	86	84	80	80
78	118	110	108	111	132	130	121	123	125	121	77	80	76	80	84	84	82	84	80	80
79	112	127	110	132	132	130	138	130	128	129	71	90	84	92	96	98	98	100	94	102
80	116	107	100	117	121	120	102	105	107	108	74	69	70	73	72	72	61	63	61	67
81	102	104	100	110	109	110	110	102	104	104	80	88	82	96	98	99	99	96	90	98
82	124	125	120	130	132	130	132	130	128	130	90	100	92	102	102	104	106	110	102	110
83	130	140	134	150	152	152	150	146	140	148	92	102	98	110	112	114	112	108	110	116
84	110	112	110	114	115	116	115	110	108	108	78	80	8	90	92	94	92	96	90	89
85	128	129	125	130	130	131	126	128	120	122	86	98	90	102	110	108	108	100	90	100
86	132	130	130	132	131	132	135	130	128	130	92	99	90	100	106	104	104	102	100	98
87	112	124	120	148	140	144	150	152	138	143	89	98	98	107	110	108	108	106	99	110
88	120	122	116	122	123	124	122	116	118	118	82	88	80	90	98	98	96	90	90	94
89	136	130	126	136	132	132	136	134	130	130	90	98	92	111	112	110	98	99	90	103
90	108	110	100	110	102	104	108	108	100	102	74	78	78	82	88	90	84	80	85	88

S.NO	MEAN ARTERIAL PRESSURE										VISUAL ANALOG SCORE						RAMSAY SEDATION						FENTANYL [µg]	COMPLICATIONS		
	PREOP	AI		AP					PR	AE	PREOP	AE	HOURS				PREOP	AE	HOURS					NAUSEA	VOMITING	DROWSINESS
		1 MIN	5 MIN	1 MIN	5 MIN	15 MIN	30 MIN	45 MIN					1	2	4	6			1	2	4	6				
1	89	115	97	121	115	121	100	98	91	112	2	5	6	6	5	6	1	1	1	1	2	2	150	A	A	A
2	100	106	100	113	115	115	105	106	101	94	2	5	6	7	6	5	1	2	2	2	1	1	140	A	A	A
3	103	134	107	131	133	133	119	107	99	121	1	4	5	6	6	6	1	1	2	1	1	2	160	A	A	A
4	98	111	102	118	112	113	102	102	92	120	2	4	5	6	6	6	1	1	1	2	1	1	150	A	A	A
5	89	113	101	120	115	114	111	107	98	115	1	5	6	7	6	6	1	1	2	1	2	2	160	A	P	A
6	101	121	109	129	125	126	122	114	103	123	1	5	5	6	5	5	1	1	1	2	1	1	160	A	A	A
7	87	101	95	107	104	105	103	104	99	105	1	5	5	7	6	6	1	2	2	1	2	2	150	A	A	A
8	96	113	106	116	113	113	113	107	105	106	2	6	6	7	6	5	1	2	1	2	2	1	140	A	A	A
9	78	100	91	108	110	112	109	105	97	109	2	5	5	6	6	6	1	1	1	1	2	2	170	A	A	A
10	88	101	99	109	111	113	96	93	95	106	2	5	5	7	6	6	1	1	2	2	2	1	200	A	P	P
11	99	105	100	109	107	109	107	103	103	106	1	6	6	7	7	7	1	2	2	2	2	2	100	A	A	A
12	87	99	93	103	103	105	103	99	96	105	1	6	5	6	6	6	1	2	2	2	2	2	120	A	A	A
13	100	109	101	113	107	108	109	103	94	103	2	6	6	7	7	7	1	3	3	2	2	2	100	A	A	A
14	93	120	105	129	127	126	122	113	102	110	2	7	6	6	5	6	1	1	2	2	2	2	150	P	A	A
15	86	98	94	109	108	109	109	106	101	107	1	5	5	6	6	6	1	1	1	1	2	2	150	A	A	P
16	93	105	100	116	119	121	124	115	109	114	1	6	5	6	5	5	1	1	1	2	2	2	120	A	A	A
17	101	117	103	118	115	115	108	103	97	115	2	5	5	5	6	6	1	3	3	2	2	2	140	A	A	A
18	93	130	102	125	130	129	123	117	104	114	1	6	7	7	6	6	1	1	2	2	2	2	140	A	A	A
19	87	129	111	133	125	122	109	81	79	121	1	6	5	6	6	6	1	1	1	1	2	2	160	A	A	A
20	81	90	87	101	93	99	87	79	85	94	1	5	6	7	6	5	1	1	2	1	2	2	160	A	P	A
21	93	122	107	125	113	113	103	103	94	112	2	5	6	6	6	6	1	1	1	1	2	1	170	A	A	A
22	94	116	107	129	123	121	117	113	105	119	1	5	6	7	6	6	1	1	1	1	2	2	160	P	A	A
23	103	127	115	127	114	114	110	107	96	127	2	5	6	6	6	6	1	1	1	2	1	2	200	A	A	A
24	87	130	103	131	118	117	107	104	97	119	1	5	6	7	6	6	1	2	2	2	1	2	180	A	A	A
25	97	114	104	119	112	110	119	113	108	111	1	5	6	7	6	6	1	1	1	2	1	1	190	A	A	A
26	100	110	99	117	115	115	109	106	101	117	2	5	6	6	7	6	1	3	3	2	2	2	100	P	A	A
27	90	107	99	115	113	115	110	109	99	111	2	6	7	7	5	5	1	1	1	1	2	2	120	A	A	A
28	85	96	93	108	107	109	108	102	96	106	1	4	6	6	5	6	1	1	2	2	2	2	120	A	A	A
29	99	113	106	127	127	125	117	111	104	114	2	5	5	5	5	5	1	3	3	2	2	2	120	A	A	P
30	96	108	98	120	115	114	113	113	100	112	1	4	5	5	6	6	1	1	1	2	2	2	150	A	A	A
31	88	88	87	92	93	95	86	87	83	85	0	1	2	3	2	3	2	3	3	3	3	3	10	A	A	A
32	98	91	90	99	98	100	101	99	91	93	0	1	2	2	3	3	2	3	4	3	3	3	10	A	A	A
33	86	88	86	92	91	94	89	89	84	86	1	2	2	3	2	2	3	2	4	2	3	2	20	A	A	A
34	87	89	84	87	89	91	90	87	83	85	1	1	2	3	3	3	2	2	3	3	3	3	20	A	P	P
35	87	85	85	88	89	91	88	88	84	84	1	2	2	2	2	2	2	3	4	3	3	3	40	A	A	P
36	98	96	93	97	99	103	100	98	93	95	1	1	2	2	2	3	2	2	3	3	3	3	40	A	A	A
37	108	109	107	109	109	107	109	109	105	103	1	2	2	3	3	2	2	3	4	3	3	3	30	A	A	P
38	97	97	97	99	101	101	99	97	93	92	0	1	2	2	2	3	2	2	3	3	3	2	30	A	A	P
39	97	99	95	100	98	97	97	99	95	97	1	2	2	2	2	2	2	3	4	3	2	3	30	P	A	A
40	97	95	95	95	99	99	99	98	94	95	0	1	2	2	2	3	2	3	4	3	3	3	20	A	A	A
41	74	74	73	79	84	85	83	83	76	75	0	2	2	2	2	3	3	3	3	2	3	3	20	A	A	A
42	88	92	87	88	91	90	87	89	85	79	1	1	2	2	3	3	2	2	3	3	3	3	30	P	A	A
43	79	79	80	85	88	88	84	85	81	83	1	2	2	3	2	3	2	3	4	2	3	2	40	A	A	P
44	77	73	74	78	81	82	82	78	73	75	0	1	2	2	2	2	3	3	3	3	3	3	20	A	A	P
45	88	87	87	93	94	93	92	93	89	87	0	2	1	2	2	3	3	2	4	3	3	2	20	A	A	A
46	85	86	86	87	90	90	91	89	86	85	0	2	1	3	3	2	2	3	3	2	2	2	30	P	P	A
47	97	97	95	100	99	99	102	96	95	94	1	1	3	3	3	3	3	3	4	3	3	3	20	A	A	P
48	84	82	80	84	89	88	85	85	83	84	1	2	3	2	2	3	2	2	4	3	3	2	20	A	A	A
49	90	90	91	91	93	91	87	89	85	83	1	2	2	2	2	3	2	3	3	3	3	3	40	A	A	P
50	90	89	85	88	89	90	89	91	85	85	1	1	2	3	3	2	3	3	3	3	3	3	30	A	A	P
51	101	97	95	99	100	100	101	99	99	99	1	1	2	2	2	2	2	3	3	3	3	3	20	P	A	A
52	103	100	100	102	105	104	104	101	100	100	1	1	2	2	2	2	2	3	4	3	3	3	20	A	P	P
53	95	93	90	95	94	95	95	95	91	92	1	2	2	3	3	2	3	2	4	3	3	3	20	A	A	P
54	93	93	89	89	93	93	91	92	86	88	1	1	2	2	2	2	3	2	4	3	3	3	20	A	P	A
55	80	77	76	82	85	87	82	83	78	80	1	2	2	3	2	2	2	3	3	2	3	2	10	P	P	A
56	90	91	91	89	95	95	96	90	90	90	1	3	3	3	2	3	3	2	4	3	3	3	60	A	A	P
57	96	90	90	96	97	99	97	94	90	89	2	3	3	3	2	2	2	3	3	4	4	4	50	A	A	A
58	79	77	77	82	84	86	85	84	78	79	1	3	3	3	2	2	2	2	4	3	3	3	60	A	A	A

S.NO	MEAN ARTERIAL PRESSURE										VISUAL ANALOG SCORE						RAMSAY SEDATION						FENTANYL [µg]	COMPLICATIONS		
	PREOP	AI		AP					PR	AE	PREOP	AE	HOURS				PREOP	AE	HOURS					NAUSEA	VOMITING	DROWSINESS
		1 MIN	5 MIN	1 MIN	5 MIN	15 MIN	30 MIN	45 MIN					1	2	4	6			1	2	4	6				
59	86	86	82	92	92	94	94	92	88	90	2	3	3	3	3	3	2	2	4	3	4	4	30	A	A	A
60	103	105	101	104	105	103	105	104	100	99	1	3	2	3	2	3	3	2	4	3	3	3	70	A	A	P
61	87	99	95	96	99	100	95	92	92	94	2	3	3	4	4	4	1	2	2	2	2	2	80	A	A	A
62	89	101	90	103	99	101	109	105	103	107	1	3	3	3	4	4	2	2	3	3	2	2	60	A	A	A
63	88	98	95	99	104	103	100	102	95	105	2	3	2	4	4	5	2	3	3	3	3	3	40	A	A	A
64	98	126	107	134	131	132	131	133	123	121	1	3	3	3	4	4	1	2	2	2	2	2	40	A	P	A
65	84	92	86	95	97	99	100	97	94	93	2	4	3	4	4	4	1	2	3	3	3	3	30	A	A	A
66	99	109	101	113	115	114	115	117	110	116	1	4	3	3	4	4	2	2	2	2	2	2	50	A	A	A
67	88	95	90	98	99	99	100	95	94	96	2	3	3	4	4	4	2	2	2	3	3	3	40	A	A	A
68	99	108	103	110	112	111	104	101	102	105	1	4	3	4	4	4	3	3	3	3	2	2	60	A	A	A
69	95	106	100	107	104	105	106	102	108	105	1	3	2	4	5	4	2	3	3	3	3	3	50	A	A	A
70	96	101	97	107	106	106	107	103	100	105	2	3	3	3	4	5	2	2	2	2	2	1	70	A	A	A
71	91	99	92	100	101	100	104	99	95	105	2	3	3	4	5	4	2	3	3	3	3	4	40	P	A	A
72	82	85	83	90	92	92	91	92	89	90	1	3	3	3	4	4	2	2	3	3	3	3	40	A	A	A
73	85	92	91	103	109	109	109	108	103	112	2	3	3	3	4	4	2	2	2	2	1	1	60	A	A	A
74	89	95	89	99	102	101	100	100	97	95	1	3	3	4	4	4	1	1	1	2	2	2	50	A	A	A
75	97	105	99	107	107	108	107	106	100	103	2	3	3	3	4	4	1	2	2	2	1	1	60	A	A	A
76	99	100	100	103	105	106	105	103	98	100	1	3	3	3	4	4	2	3	2	1	1	1	40	A	A	A
77	99	101	96	98	98	100	97	96	94	96	2	3	3	3	4	4	2	2	3	3	2	1	50	A	A	A
78	91	90	87	90	100	99	95	97	95	94	1	3	2	3	4	4	1	2	2	2	1	1	30	A	A	A
79	85	102	93	105	108	109	111	110	105	111	2	3	3	4	4	4	2	2	2	3	3	3	50	A	A	A
80	88	82	80	88	88	88	75	77	76	81	1	3	3	4	5	4	1	2	2	2	1	1	60	A	A	A
81	87	93	88	101	102	103	103	98	95	100	1	3	3	3	3	3	2	2	1	1	1	1	80	A	A	P
82	101	108	101	111	112	113	115	117	111	117	2	3	3	4	4	4	2	2	2	2	1	1	100	A	A	P
83	105	115	110	123	125	127	125	121	120	127	1	2	2	2	3	4	1	1	2	2	2	1	60	A	P	P
84	89	91	42	98	100	101	100	101	96	95	2	2	2	3	3	3	3	3	2	2	2	1	60	A	A	A
85	100	108	102	111	117	116	114	109	100	107	2	2	2	3	3	3	3	3	2	2	1	1	120	P	P	P
86	105	109	103	111	114	113	114	111	109	109	1	2	2	2	3	3	2	2	2	1	1	1	100	A	A	P
87	97	107	105	121	120	120	122	121	112	121	2	2	3	3	3	4	1	1	1	2	2	2	80	A	A	A
88	95	99	92	101	106	107	105	99	99	102	2	3	3	4	4	4	2	2	2	3	3	2	80	A	A	A
89	105	109	103	119	119	117	111	111	103	112	2	3	3	4	4	4	2	2	2	1	1	1	60	A	A	A
90	85	89	85	91	93	95	92	89	90	93	2	2	2	3	3	3	1	2	2	2	1	1	40	A	A	A